Understanding Lymphoma and Chronic Lymphocytic Leukemia (CLL)

Burkitt Lymphoma

Lymphoma Research Foundation

Burkitt lymphoma (BL) is a rare but very *aggressive* (fast-growing) form of mature (fully developed) B-cell non-Hodgkin lymphoma (NHL).

The disease typically involves younger patients and is the most common type of pediatric (in children from birth to young adulthood) NHL. It may also be seen in elderly patients. It may affect different parts of the body, such as the bowel, kidneys, jaw, bones, or ovaries. In some cases, it may spread to the central nervous system (CNS, the brain and spinal cord). At diagnosis, a sample of cerebrospinal fluid (the fluid that flows in and around the CNS) may be taken to determine if the disease has spread to the CNS.

There are three main types of BL:

- Endemic BL typically affects boys between the ages of 4 and 7 years in specific parts of the world (Equatorial Africa, Papua New Guinea, and regions of South America), where it is the most common childhood cancer. Endemic BL is linked to infection with Epstein-Barr virus (EBV, the virus that causes mononucleosis, or "mono") and is rare outside these specific areas. However, the majority of people who have EBV infection will not develop endemic BL.
- Sporadic BL occurs in children and adults worldwide. It makes up about 1-2% of NHLs in adults and is one of the most common types of childhood lymphoma in the US.
- Immunodeficiency-associated BL is most common in people with human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS, a condition where the immune system is weakened and unable to fight common infections). This type of BL can also occur in patients who have inherited immune deficiencies or who take immunosuppressive medications to prevent rejection after organ transplant, or other reasons. However, most people with these conditions will not develop immunodeficiency-associated BL.

The cancer cells in BL have a permanent change (genetic mutation) in a part of their DNA (deoxyribonucleic acid, the molecule that carries the genetic information inside the cell) called a translocation (Figure 1) of the MYC gene. This translocation is only found in the lymphoma cells (not on healthy cells) and is used to diagnose the disease. In adults, BL is sometimes difficult to distinguish (tell apart) from different types of NHL called high grade B-cell lymphoma (HGBCL) or diffuse large B-cell lymphoma (DLBCL)—a more common form of aggressive B-cell NHL. It is very important for doctors to distinguish BL from HGBCL and DLBCL, because each disease is treated differently. For more information about DLBCL, please view the *Diffuse Large B-Cell Lymphoma* fact sheet on the Foundation's website (lymphoma.org/publications).

For more information about BL, please view the *Understanding Lymphoma and CLL Guide* on the Foundation's website (visit lymphoma.org/publications).

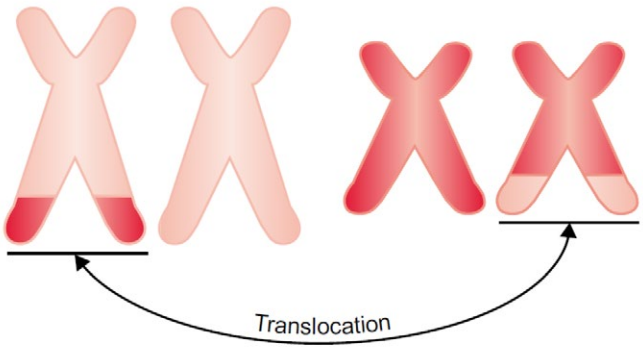

Figure 1: Translocation of the MYC gene, where a chromosome breaks and part of it reattaches to another chromosome.

Treatment Options

Because BL is very aggressive, diagnosis is often a medical emergency, requiring urgent hospitalization and treatment. The choice of initial therapy depends on different factors, such as:

- The patient's age.
- The presence of other medical conditions (sometimes referred to as co-morbidities).
- Disease stage (how much the cancer has grown and if it has spread to other parts of the body).
- Risk level of BL (low-risk to high-risk). Doctors determine the risk level based on the results of tests and scans, and on how the disease is affecting the patient's daily life.

Types of treatment for BL can include:

- Chemoimmunotherapy which is a combination of chemotherapy (drugs that stop the growth of or kill cancer cells) with immunotherapy (drugs that use the body's immune system to fight cancer)
- Immunotherapy, including:
  - Monoclonal antibodies (proteins made in the laboratory that bind to markers at the surface of cancer cells and helps the body fight cancer)

BL is usually very responsive to intensive (given at high doses or over several months) combination chemotherapy regimens and cure rates (the percentage of patients who get cured from the cancer) are high. Therefore, standard of care (the proper treatment that is widely used by healthcare professionals and accepted by medical experts) treatment typically involves short courses of intensive chemotherapy regimens in combination with the monoclonal antibody rituximab (Rituxan). Less intensive regimens might be used for patients with low-risk BL or who are not fit for intensive chemotherapy.

Specific chemotherapy treatment options for adults include the regimens listed in **Table 1.**

Patients with BL that has spread to the central nervous system (CNS), also referred to as CNS involvement, are at a higher risk of relapse (disease returns after treatment). Patients with BL without CNS involvement require prophylaxis (preventive treatment) to make sure that the disease will not affect the CNS later on. How often a person needs treatment, which is administered (given) intrathecally (injected into the spinal fluid), depends on whether or not there is CNS involvement at diagnosis.

Immunodeficiency-associated BL should be treated with similar regimens as for HIV-negative patients with BL. Antiretroviral therapy (drugs used to treat HIV infection) can be safely administered with chemotherapy.

Table 1: Common Intensive Chemotherapy Regimens Used to Treat Burkitt Lymphoma

Chemotherapy regimens	Agents (Drugs)
Dose-adjusted EPOCH-R (DA EPOCH-R)	• Etoposide (Etopophos, Toposar, VePesid), prednisone, vincristine (Oncovin, Vincasar), cyclophosphamide, and doxorubicin plus rituximab (Rituxan). • Intrathecal (injected into the cerebrospinal fluid) methotrexate for patients who are at low risk and without CNS involvement, or high- risk patients who are not able to tolerate more aggressive treatments.
HyperCVAD	• Cyclophosphamide, vincristine, doxorubicin, and dexamethasone alternating with high-dose methotrexate and cytarabine (Cytosar). • If rituximab (Rituxan) is added, the regimen is called R+HyperCVAD. • Intrathecal therapy may be given for a longer duration than the other treatments listed herein.
CODOX-M	• Cyclophosphamide, doxorubicin, and vincristine with intrathecal methotrexate and cytarabine, followed by high-dose systemic (throughout the body) methotrexate with or without rituximab, for three cycles. • This regimen is sometimes alternated with IVAC (ifosfamide, intrathecal methotrexate, etoposide, and high-dose cytarabine).
CALGB	• Cyclophosphamide, prednisone, ifosfamide, methotrexate, vincristine, cytarabine, etoposide, doxorubicin, and dexamethasone. • If rituximab (Rituxan) is added, the regimen is called R+CALGB. • Outcomes improved for R+CALGB.
LMB	• Cyclophosphamide, doxorubicin, vincristine, and prednisone. • If rituximab (Rituxan) is added, the regimen is called R+LMB. • Intermediate or high-risk groups may additionally receive regimens including cytarabine, methotrexate, and etoposide.

BL, Burkitt lymphoma; CNS, central nervous system.

Different combination chemotherapy regimens are used to treat BL in children and adolescents, and younger patients tend to have both excellent responses to chemotherapy and high cure rates. This means that the cancer disappears after treatment and does not come back. These patients are now treated with smaller amounts of chemotherapy, which can still cure the disease but have fewer side effects.

Patients with BL that are being treated may experience tumor lysis syndrome. This means that a large number of cancer cells die in a short amount of time after treatment and flood the bloodstream with toxins, which may damage the kidneys, heart and liver. Symptoms may include:

- Nausea and vomiting.
- Shortness of breath.
- Irregular heartbeat.
- Clouding of the urine.
- Lethargy (feeling drowsy and without energy).
- Joint discomfort.

This condition is potentially severe and can occur spontaneously or after chemotherapy. Tumor lysis syndrome can cause organ damage, 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, and Zyloprim) or rasburicase (Elitek). It is very important that patients talk to their doctor if they experience any of the symptoms listed above.

Treatments Under Investigation

Many new treatments (also called investigational drugs) and combinations are currently being tested in clinical trials for patients with BL. This includes patients who are newly diagnosed and those with relapsed (disease comes back after treatment) or refractory (disease does not respond to treatment) BL. Participation in a clinical trial is highly encouraged when available. Results from these clinical trials may improve or change the current standard of care. Table 2 (below) lists some of these investigational drugs that can be accessed through a clinical trial. For more information on clinical trials, view the *Understanding Clinical Trials* fact sheet on the Foundation's website (lymphoma.org/publications).

Table 2: Investigational drugs for newly diagnosed Burkitt Lymphoma

Agent (drug)	Class (type of treatment)
Brexucabtagene Autoleucel (Tecartus)	CAR T cell therapy; anti-CD19
Nivolumab (Opdivo)	Immune checkpoint inhibitor; anti-PD-1
Pembrolizumab (Keytruda)	Immune checkpoint inhibitor; anti-PD-1
Ofatumumab (Arzerra)	Monoclonal antibody; anti-CD20
IMT-009	Monoclonal antibody; anti-CD161
Venetoclax (Venclexta)	Targeted therapy. Bcl-2 inhibitor
Ibrutinib (Imbruvica)	Targeted therapy; BTK inhibitor
Obinutuzumab (Gazyva)	Monoclonal antibody; anti-CD20
Lenalidomide (Revlimid)	Immunomodulator drug
Acalabrutinib (Calquence)	Targeted therapy; BTK inhibitor
Inotuzumab ozogamicin (Besponsa)	Antibody-drug conjugate; anti-CD22
Polatuzumab vedotin (Polivy)	Antibody-drug conjugate; anti-CD79b
Sepantronium bromide (PC-002)	Targeted therapy; IAP inhibitor
Bortezomib (Velcade)	Targeted therapy; proteosome inhibitor
Blinatumomab (Blincyto)	Bispecific antibody; anti-CD3 and CD19

Bcl-2, B-cell lymphoma-2; BL, Burkitt lymphoma; BTK, Bruton's kinase; CAR: chimeric antigen receptor; IAP, inhibitor of apoptosis; PD-1, programmed death receptor-1.

Clinical Trials

Clinical trials are important in finding both drugs that are effective and the best treatment doses for patients with lymphoma. Patients interested in participating in a clinical trial should view the *Understanding Clinical Trials* fact sheet on the Foundation's website (visit **lymphoma.org/publications**), and the *Clinical Trials Search Request Form* at lymphoma.org, talk to their physician, or contact the Foundation's 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. During these visits, medical tests (like computed tomography [CT] or positron emission tomography [PET] scans) may be required to evaluate the need for additional treatment.

Some treatments can cause *long-term* side effects (occur **during** treatment and continue for months or years) or late side effects (appear only months, years or decades **after** treatment has ended). These can vary depending on the following factors:

- Duration of treatment (how long the treatment has lasted)
- Frequency of treatment (how often the treatment was administered)
- Type of treatment given
- Patient's age and gender
- Patient's overall health at the time of treatment.

A physician will check for these effects during follow-up care. Visits may become less frequent the longer the patient stays in remission (lack of signs and symptoms of disease).

Patients and their care partners are encouraged to keep copies of all medical records. This includes test results as well as information on the types, amounts, and duration of all treatments received. Medical records are important for keeping track of any side effects resulting from treatment or potential disease recurrences. The Foundation's award-winning *Focus On Lymphoma* mobile app and Lymphoma Care Plan (**lymphoma.org/publications**) can help patients manage this documentation.

Lymphoma Care Plan

Keeping your information in one location can help you feel more organized and in control. This also makes it easier to find information pertaining to your care and saves valuable time. The Foundation's Lymphoma Care Plan document organizes information on your health care team, treatment regimen, and follow-up care. You can also keep track of health screenings and any symptoms you experience to discuss with your health care provider during future appointments. The Lymphoma Care Plan document can be accessed by visiting **lymphoma.org/publications**.

Patient Education Programs

The Foundation also offers a variety of educational activities, including live meetings and webinars for individuals looking to learn directly from lymphoma experts. These programs provide the lymphoma community with important information about the diagnosis and treatment of lymphoma, as well as information about clinical trials, research advances and how to manage/cope with the disease. These programs are designed to meet the needs of a lymphoma patient from the point of diagnosis through long-term survivorship. To view our schedule of upcoming programs, please visit **lymphoma.org/programs**.

Helpline

The Foundation's Helpline staff are available to answer your general questions about lymphoma 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. The Foundation also offers a one-to-one peer support program called the Lymphoma Support Network and clinical trials information through our Clinical Trials Information Service. For more information about any of these resources, visit our website at **lymphoma.org**, or contact the Helpline at **(800) 500-9976** or **helpline@lymphoma.org**.

Para información en Español, por favor visite **lymphoma.org/es**. (For Information in Spanish please visit **lymphoma.org/es**).

Focus on Lymphoma Mobile App

Focus on Lymphoma is the first app to provide patients and their care partners with tailored content based on lymphoma subtype, and actionable tools to better manage diagnosis and treatment. Comprehensive lymphoma management, conveniently in one secure and easy-to-navigate app, no matter where you are on the care continuum. Get the right information, first, with resources from the entire Lymphoma Research Foundation content library, use unique tracking and reminder tools, and connect with a community of specialists and patients. To learn more about this resource, visit our website at **lymphoma.org/mobileapp**, or contact the Foundation's Helpline at **(800) 500-9976** or **helpline@lymphoma.org**.

Lymphoma Research Foundation

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