

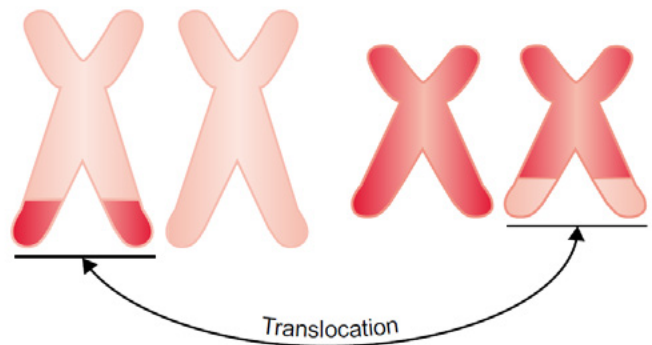
# Understanding Lymphoma: Burkitt Lymphoma

**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. BL 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 for 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 a different type of NHL called 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 DLBCL because each disease is treated differently. For more information about DLBCL, please view the *Diffuse Large B-Cell Lymphoma* fact sheet on Lymphoma Research Foundation’s website ([lymphoma.org/publications](http://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. However, BL is usually very responsive to intensive combination chemotherapy regimens (anticancer drugs given at high doses or over several months), and cure rates (the percentage of patients who get cured from the cancer) are high.

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

Standard of care (the proper treatment that is widely used by health care professionals and accepted by medical experts) treatment typically involves short courses of intensive chemotherapy regimens in combination with rituximab (Rituxan). Less intensive regimens might be used for patients with low-risk BL or who are not fit for intensive chemotherapy. Specific treatment options for adults include the regimens listed in Table 1.

**Table 1. Common Intensive Chemotherapy Regimens Used to Treat Patients with BL.**

Chemotherapy regimens	Agents (Drugs)
<b>Dose-adjusted EPOCH-R (DA EPOCH-R)</b>	<ul style="list-style-type: none"> <li>• Etoposide (Etopophos, Toposar, VePesid), prednisone, vincristine (Oncovin, Vincasar), cyclophosphamide, and doxorubicin plus rituximab (Rituxan)</li> <li>• 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</li> </ul>
<b>HyperCVAD</b>	<ul style="list-style-type: none"> <li>• Cyclophosphamide, vincristine, doxorubicin, and dexamethasone alternating with high-dose methotrexate and cytarabine (Cytosar)</li> <li>• If rituximab (Rituxan) is added, the regimen is called R+HyperCVAD</li> <li>• Intrathecal therapy may be given for a longer duration than the other treatments listed herein</li> </ul>
<b>CODOX-M</b>	<ul style="list-style-type: none"> <li>• 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</li> <li>• This regimen is sometimes alternated with IVAC (ifosfamide, intrathecal methotrexate, etoposide, and high-dose cytarabine)</li> </ul>
<b>CALGB</b>	<ul style="list-style-type: none"> <li>• Cyclophosphamide, prednisone, ifosfamide, methotrexate, vincristine, cytarabine, etoposide, doxorubicin, and dexamethasone</li> <li>• If rituximab (Rituxan) is added, the regimen is called R+CALGB</li> <li>• Outcomes improved for R+CALGB</li> </ul>
<b>LMB</b>	<ul style="list-style-type: none"> <li>• Cyclophosphamide, doxorubicin, vincristine, and prednisone</li> <li>• If rituximab (Rituxan) is added, the regimen is called R+LMB</li> <li>• Intermediate or high-risk groups may additionally receive regimens including cytarabine, methotrexate, and etoposide</li> </ul>

BL, Burkitt lymphoma; CNS, central nervous system.

Patients with BL that has spread to the 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 (given) with chemotherapy.

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 who 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 Lymphoma Research Foundation's website ([lymphoma.org/publications](http://lymphoma.org/publications)).

**Table 2. Treatments Under Investigation for Treatment of BL in Phase 2 or 3 Clinical Trials.**

Agent (Drug)	Class (Type of treatment)
<b>Tisagenlecleucel (Kymriah)</b>	• CAR T-cell therapy; anti-CD19
<b>Brexucabtagene Autoleucel (Tecartus)</b>	• CAR T-cell therapy; anti-CD19
<b>Nivolumab (Opdivo)</b>	• Immune checkpoint inhibitor; anti-PD-1
<b>Pembrolizumab (Keytruda)</b>	• Immune checkpoint inhibitor; anti-PD-1
<b>Ofatumumab (Arzerra)</b>	• Monoclonal antibody; anti-CD20
<b>IMT-009</b>	• Monoclonal antibody; anti-CD161
<b>Venetoclax (Venclexta)</b>	• Targeted therapy; Bcl-2 inhibitor
<b>Ibrutinib (Imbruvica)</b>	• Targeted therapy; BTK inhibitor
<b>Obinutuzumab (Gazyva)</b>	• Monoclonal antibody; anti-CD20
<b>Lenalidomide (Revlimid)</b>	• Immunomodulator drug
<b>Acalabrutinib (Calquence)</b>	• Targeted therapy; BTK inhibitor
<b>Inotuzumab ozogamicin (Besponsa)</b>	• Antibody-drug conjugate; anti-CD22
<b>Polatuzumab vedotin (Polivy)</b>	• Antibody-drug conjugate; anti-CD79b
<b>Sepantronium bromide (PC-002)</b>	• Targeted therapy; IAP inhibitor
<b>Vorinostat (Zolinza)</b>	• Targeted therapy; HDAC inhibitor

Bcl-2, B-cell lymphoma-2; BL, Burkitt lymphoma; BTK, Bruton's tyrosine kinase; CAR: chimeric antigen receptor; HDAC, histone deacetylase; 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 ([lymphoma.org/publications](http://lymphoma.org/publications)) and the *Clinical Trials Search Request Form* ([lymphoma.org](http://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](mailto:helpline@lymphoma.org).

## FOLLOW-UP

Patients with lymphoma should have regular visits with their physician. During these visits, medical tests (such as blood tests and computed tomography [CT] scans) may be required to evaluate the need for additional treatment.

Patients and their caregivers are encouraged to keep copies of all medical records, including 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.

## LYMPHOMA CARE PLAN AND PATIENT EDUCATION PROGRAMS

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. LRF'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](http://lymphoma.org/publications). LRF also offers a variety of educational activities, including live meetings and webinars, for individuals looking to learn directly from lymphoma experts. To view our schedule of upcoming programs, please visit [lymphoma.org/programs](http://lymphoma.org/programs).

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## LRF Helpline

The LRF 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. LRF 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](http://lymphoma.org), or contact the LRF Helpline at **(800) 500-9976** or [helpline@lymphoma.org](mailto:helpline@lymphoma.org).

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

## LRF FOCUS ON LYMPHOMA MOBILE APP

*Focus on Lymphoma* is the first app to provide patients and their caregivers with tailored content based on lymphoma subtype and actionable tools to better manage diagnosis and treatment. It provides convenient and comprehensive lymphoma management 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](http://lymphoma.org/mobileapp), or contact the LRF Helpline at **800-500-9976** or [helpline@lymphoma.org](mailto:helpline@lymphoma.org).

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