LYMPHOMA RESEARCH • FOUNDATION

Understanding Lymphoma
Burkitt Lymphoma

Burkitt lymphoma (BL) is a rare but highly aggressive (fast-growing) form of mature B-cell non-Hodgkin lymphoma (NHL). The disease typically involves younger patients and represents the most common type of pediatric NHL. It also may be seen in elderly patients as well. It may affect the jaw, bones of the face, bowel, kidneys, ovaries, and in some cases, it 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.

Patients with BL may experience tumor lysis syndrome, which occurs when tumor cells release their contents into the bloodstream. Symptoms may include nausea and vomiting, shortness of breath, irregular heartbeat, clouding of the urine, lethargy, or joint discomfort. This condition is potentially severe and can occur spontaneously or after chemotherapy. Tumor lysis syndrome can cause kidney and heart 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, Zyloprim) or rasburicase (Elitek).

There are three main types of BL: endemic, sporadic, and immunodeficiency-associated.

- Endemic BL typically affects boys between the ages of 4 and 7 years in specific geographic areas (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) and is rare outside these specific areas.
- Sporadic BL occurs in children and adults worldwide. It accounts for about one to two percent of NHLs in adults and is one of the most common types of childhood lymphoma in the US.
- The immunodeficiency-related variety of BL is most common in people with human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS). Immunodeficiency-related BL can also occur in patients who have inherited immune deficiencies or who take immunosuppressive medications to prevent rejection after organ transplant.

A genetic alteration (called translocation) of the *MYC* gene in the lymphoma cells (not the genes that you inherit) is a hallmark of BL, making this an important finding for diagnosis of the disease. In adults, BL is sometimes difficult to distinguish from diffuse large B-cell lymphoma (DLBCL)—a more common form of aggressive mature B-cell NHL. Accurately distinguishing between BL and DLBCL is critical, because each disease is treated differently.

TREATMENT OPTIONS

Because BL is extremely aggressive, diagnosis is frequently a medical emergency, requiring urgent hospitalization and rapid treatment. However, BL is often very responsive to intensive combination chemotherapy regimens and cure rates are high.

The choice of initial therapy depends on different factors, such as age, the presence of other medical conditions, stage, and risk level of BL. Standard of care treatment typically involves short courses of aggressive 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 following regimens:

The Dose-Adjusted EPOCH (DA EPOCH-R) regimen includes:

- Etoposide (Etopophos, Toposar, VePesid), prednisone, vincristine (Oncovin, Vincasar), cyclophosphamide, and doxorubicin plus rituximab (Rituxan)
- Intrathecal 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

The HyperCVAD (R+HyperCVAD) regimen includes:

- Cyclophosphamide, vincristine, doxorubicin, and dexamethasone alternating with high-dose methotrexate and cytarabine (Cytosar) plus rituximab
- Intrathecal therapy may be given for a longer duration than the other treatments listed herein

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)

The CALGB (R+CALGB) regimen includes:

- Cyclophosphamide, prednisone, ifosfamide, methotrexate, vincristine, cytarabine, etoposide, doxorubicine, and dexamethasone
- Outcomes improved when rituximab (Rituxan) was added to the above regimen

The LMB (R+LMB) regimen includes:

- Cyclophosphamide, doxorubicin, vincristine, and prednisone
- Intermediate or high-risk groups may additionally receive regimens including cytarabine, methotrexate, and etoposide

CNS involvement is the strongest risk factor for *relapse* (disease returns after treatment). Patients with BL without CNS involvement require prophylaxis (preventive treatment). The frequency of these treatments, which are given intrathecally (injected into the spinal fluid), depends on whether or not CNS involvement is present at diagnosis.

HIV-related BL should be treated with similar regimens as for HIV-negative patients with BL. Antiretroviral therapy can be safely administered with chemotherapy. Different combination chemotherapy regimens are used to treat BL in children and adolescents, and younger patients tend to have both excellent chemotherapy responses 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 combined with the agents mentioned above. Participation in a clinical trial is highly encouraged when available. New agents are also being investigated alone or as part of combination therapy in relapsed or refractory (does not respond to treatment) disease, including the following:

- Tisagenlecleucel (Kymriah)
- Devimistat (CPI-613)
- Nivolumab (Opdivo) with lenalidomide (Revlimid)
- Ofatumumab (Arzerra) with DA EPOCH
- Obinutuzumab (Gazyva) with ICE (ifosfamide, carboplatin and etoposide)
- Venetoclax (Venclexta) with ibrutinib (Imbruvica), prednisone, obinutuzmab (Gazyva) and lenalomide (Revlimid)
- Acalabrutinib (Calquence) with pembrolizumab (Keytruda)
- Sepantronium bromide (PC-002)
- Clofarabine (Clolar, Evoltra) and mitoxantrone (Novantrone)
- Vorinostat (Zolinza) with chemotherapy

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 (visit **lymphoma.org/publications**), 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 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 (disappearance of signs and symptoms) 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 BL, 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 BL, 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. 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 BL. LRF also provides many educational activities, including our in- person meetings and webinars for people with lymphoma. For more information about any of these resources, visit our websites at **lymphoma.org/burkitt** or **lymphoma.org**, or contact the LRF Helpline at **(800) 500-9976** or **helpline@lymphoma.org**.

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