

Understanding Lymphoma

High-Grade B-Cell Lymphoma

High-grade B-cell lymphoma (HGBL) is a category of B-cell non-Hodgkin lymphoma (NHL) introduced in 2008 by the World Health Organization (WHO). This type of lymphoma is *aggressive* (fast-growing) and can be grouped in two subtypes:

- **HGBL with *MYC* and *BCL2* and/or *BCL6* translocations.** This subtype is characterized by specific genetic changes called *translocations* in the *MYC* and *BCL2* and/or *BCL6* genes. This category includes all NHL previously known as double/triple hit lymphoma. An estimate of 20-35% cases of diffuse large B-cell lymphoma (DLBCL) over-express *MYC* and *BCL2* proteins (called “double expressor lymphoma”), but do not carry translocations in *MYC* and *BCL2* and/or *BCL6*. These double-expressor DLBCL are less aggressive, often treated differently, and are not included in the HGBL category.
- **HGBL, not otherwise specified (NOS).** This subtype includes aggressive B-cell lymphomas with mixed features of both DLBCL and Burkitt lymphoma (BL), blastoid-appearing large B-cell lymphomas, and cases lacking *MYC* and *BCL2* or *BCL6* translocations.

Cancer cells in HGBL can appear similar to B-lymphoblastic leukemia/lymphoma (B-LBL), BL, and DLBCL, requiring expert hematopathology review. The signs and symptoms of HGBL may also be similar to those of DLBCL and BL. These include a painless, rapid swelling in the neck, underarms, or groin that is caused by enlarged lymph nodes. For some patients, the swelling may be painful. Other symptoms may include night sweats, fever, and unexplained weight loss. Patients may notice fatigue, loss of appetite, shortness of breath, or pain.

TREATMENT OPTIONS

HGBL is treatable, but more likely to recur than DLBCL. These lymphomas are generally treated with one of the following combination chemotherapy regimens:

- **DA-EPOCH-R** (dose-adjusted etoposide/VP16 [VePesid, Toposar, Etopophos], prednisone [Deltasone and others], vincristine [Oncovin and others], cyclophosphamide [Cytoxan, Neosar], and doxorubicin/hydroxydaunorubicin [Rubex, Adriamycin PFS] plus rituximab [Rituxan])
- **R-Hyper-CVAD/MA** (rituximab plus hyperfractionated cyclophosphamide, vincristine, doxorubicin, and dexamethasone [Decadron and others], alternating with high-dose methotrexate [Mexate and others] and cytarabine/high-dose Ara-C [Cytosar-U, Tarabine PFS])
- **R-CODOX-M/R-IVAC** (rituximab plus cyclophosphamide, vincristine, doxorubicin, and methotrexate, alternating with rituximab plus ifosfamide [Ifex], etoposide, and cytarabine)
- **RCHOP** (rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone)
- **Biosimilar therapies** (drugs that are modeled after an existing biologic therapy) may be an option for patients who are taking rituximab. These include rituximab-abbs and rituximab-pvvr.

Some patients with HGBL may undergo high-dose chemotherapy followed by an *autologous stem cell transplant* (patient’s own cells are infused after high-dose chemotherapy). If HGBL recurs after initial therapy, autologous stem cell transplant, CAR-T cell transplant, or *allogeneic stem cell transplant* (patients receive stem cells from a donor) may be utilized. For more information on stem cell transplantation, view the *Understanding the Stem Cell Transplantation Process* publication on LRF’s website (lymphoma.org/publications).

Compared with DLBCL, HGBL may have a higher risk of recurring in the patient’s *central nervous system* (CNS; the brain and spinal cord). To reduce this risk, some patients with HGBL may receive additional chemotherapy drugs to treat the CNS in addition to one of the chemotherapy regimens described above. CNS treatments may include methotrexate and/or cytarabine that is administered either intravenously, through a *lumbar puncture* (spinal tap) or both. A lumbar puncture is a procedure where a small needle is inserted into the back, some spinal fluid is withdrawn, and chemotherapy is injected directly into the *cerebrospinal fluid* surrounding the brain and spinal cord.

TREATMENTS UNDER INVESTIGATION

Clinical trials are underway to test new drugs in patients with HGBL. Some of these new drugs include:

- CAR-T therapy
- Pembrolizumab (Keytruda)
- Zanubrutinib (Brukinsa)
- Bi-specific T-cell engager (BiTE) therapy including epcortimab, mosunetuzumab, glofitmab, and odronextamab
- PI3kinase inhibitors
- Cyclin dependent kinase inhibitors

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 LRF for any treatment updates that may have recently emerged.

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) or talk to their physician. The LRF Helpline can also be contacted for an individualized clinical trial search by calling **(800) 500-9976**, by emailing helpline@lymphoma.org, or by submitting the *Clinical Trials Search Request Form* at 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. Medical tests (such as blood tests, computed tomography [CT] scans, and positron emission tomography [PET] scans) may be required (disappearance of signs and symptoms) to evaluate for relapse.

Some treatments can cause long-term side effects or late side effects, which can vary based on duration and frequency of treatments, age, gender, and the overall health of each patient at the time of treatment. A physician will check for these side effects during follow-up care. Visits may become less frequent the longer the disease remains in remission.

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 award-winning *Focus On Lymphoma* mobile app (lymphoma.org/mobileapp) and our *Lymphoma Care Plan* (lymphoma.org/publications) can help patients manage this documentation.

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 HGBL, 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 HGBL, 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.

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. LRF offers a Lymphoma Care Plan as a resource for patients and their caregivers. 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.

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 HGBL. 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/HGBL or lymphoma.org, or contact the LRF Helpline at (800) 500-9976 or helpline@lymphoma.org.

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