LYMPHOMA
RESEARCH • FOUNDATION

Getting the Facts

Helpline: (800) 500-9976
helpline@lymphoma.org

Double-Hit Lymphoma

Overview

Lymphoma is the most common blood cancer. The two main forms of lymphoma are Hodgkin lymphoma (HL) and non-Hodgkin lymphoma (NHL; which includes B-cell and T-cell lymphomas). 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).

Double-hit lymphoma (DHL) is a type of B-cell NHL characterized by *rearrangements* (parts of genes switch places within chromosomes) in two particular genes. One rearrangement involves the *MYC* gene, and the other involves the *BCL2* gene or, less commonly, the *BCL6* gene. If rearrangements are present in all three genes—*MYC*, *BCL2*, and *BCL6*—the condition is called "triple-hit lymphoma."

With respect to gene mutations, DHL shares many features with two other types of B-cell lymphomas—diffuse large B-cell lymphoma (DLBCL) and Burkitt lymphoma. In fact, about five percent of DLBCLs and about 32 to 78 percent of Burkitt lymphomas have rearrangements of the *MYC* and *BCL2*/*BCL6* genes and are thus called DHLs. However, note that the *morphology* (shape, structure, and form) of DHL cells is different from that of Burkitt lymphoma cells. Furthermore, research has shown that DHL differs in several important ways from the forms of DLBCL and Burkitt lymphoma that do not have dual gene rearrangements. For this reason, in 2016 the World Health Organization designated DHL as its own category of B-cell NHL.

DHL is an *aggressive* (fast-growing) lymphoma with signs and symptoms that may be similar to those of DLBCL and Burkitt lymphoma. (view the *Diffuse Large B-Cell Lymphoma* and *Burkitt Lymphoma* fact sheets on the Lymphoma Research Foundation's [LRF's] website at lymphoma.org/publications for more information). Molecular tests (such as fluorescence in situ hybridization [FISH] or immunohistochemistry [IHC]) that allow doctors to check for gene rearrangements in chromosomes under a microscope are used to confirm a diagnosis of DHL.

Treatment Options

Because DHL is a fairly new classification of lymphoma, ongoing research is helping doctors learn more about the best ways to treat this disease. DHLs 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** (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)

Some patients with DHL may undergo high-dose chemotherapy followed by either an *autologous stem cell transplant* (using the patient's own cells) or an *allogeneic stem cell transplant* (using cells from a donor). For more information on stem cell transplantation, view the *Understanding the Stem Cell Transplantation Process* publication on LRF's website at lymphoma.org/publications.

Compared with other types of B-cell lymphomas, DHL cells are more likely to spread to a patient's *central nervous system* (CNS; the brain and spinal cord). To reduce this risk, patients with DHL may receive CNS *prophylaxis* (medication to prevent a disorder) in addition to one of the combination chemotherapy regimens described above. CNS prophylaxis is administered through a *lumbar puncture* (spinal tap), which allows the doctor to inject one or more chemotherapy drugs directly into the *cerebrospinal fluid* surrounding the brain and spinal cord.

Treatments Under Investigation

Several novel individual and combination therapies are currently being studied in clinical trials for the treatment of patients with DHL, including:

- Alemtuzumab (Lemtrada) with cyclophosphamide
- Bromodomain and Extra-Terminal (BET) inhibitors including, GSK525762 and INCB057643
- Durvalumab (Imfinzi)
- Ibrutinib (Imbruvica) and bendamustine (Treanda, Bendeka)/ rituximab (Rituxan)
- Venetoclax (Venclexta) with DA-EPOCH-R

Another area of research for treating DHL includes the use of cyclin-dependent kinase (CDK) 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 at lymphoma.org/publications, 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 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 at various times during *remission* (disappearance of signs and symptoms) to evaluate the need for additional treatment.

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.

Patient and Caregiver Support Services

A lymphoma diagnosis often triggers a range of feelings and concerns. In addition, cancer treatment can cause physical discomfort. One-to-one peer support programs, such as LRF's *Lymphoma Support Network*, connect patients and caregivers with volunteers who have experience with lymphoma, similar treatments, or challenges, for mutual emotional support and encouragement. Patients and loved ones may find this information useful whether the patient is newly diagnosed, in treatment, or in remission.

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 and double-hit lymphoma. LRF also provides many educational activities, from in-person meetings to teleconferences and webcasts for people with lymphoma, as well as patient guides and e-Updates that provide the latest disease-specific news and treatment options. 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.

Contact the Lymphoma Research Foundation
Helpline: (800) 500-9976
helpline@lymphoma.org
Website: lymphoma.org

Medical reviewer:
Stephen M. Ansell, MD, PhD
Mayo Clinic, Rochester

Supported through grants from: Celgene, Genentech A Member of the Roche Group, Biogen

This fact sheet was also supported by the former Double Hit Lymphoma Foundation.

Stay Connected through our social media

Last Updated February 2018