

Understanding Lymphoma and Chemotherapy

Chemotherapy drugs work against one of the primary characteristics of cancer cells: their tendency to grow and multiply very quickly. Chemotherapy halts cell growth to prevent cancer cells from making more and more cancer cells. However, chemotherapy drugs also affect normal cells in the body that divide rapidly, such as those found in the hair follicles, blood, and mouth. This can cause side effects.

The purpose of chemotherapy is to kill cancer cells. It is commonly used to treat cancer that is systemic, meaning that the cancer may be in more than one location or has spread throughout the body. Lymphoma is caused by uncontrolled growth in one of two types of white blood cells, called T cells and B cells, both of which travel through the bloodstream. T cells and B cells are important elements of the immune system. One advantage of chemotherapy is that it can also travel in the bloodstream to kill lymphoma cells throughout the body.

Many patients who are treated for lymphoma are given two or more medications together, called combination chemotherapy. These chemotherapy drugs are combined to create a treatment regimen, which is a specific schedule that the drugs are given during certain days of each treatment cycle. The reason for using a combination of drugs is to increase how effectively the drugs kill or damage cancer cells. Since cancer cells divide more rapidly than normal cells, they are more sensitive to chemotherapy.

Oncology nurses are usually responsible for administering the chemotherapy regimen prescribed by the doctor. Most patients receive their chemotherapy in an outpatient clinic, hospital outpatient department, or physician's office, but sometimes patients need to stay in the hospital to receive their treatment. The decision to do treatment on an inpatient basis may be made due to factors such as prolonged chemotherapy infusions, or the need to monitor for certain side effects.



COMMON CHEMOTHERAPY REGIMENS FOR HODGKIN LYMPHOMA (HL) AND NON-HODGKIN LYMPHOMA (NHL)

Many chemotherapy regimens for B-cell NHL include the monoclonal antibody rituximab (Rituxan), which is an immunotherapy. Rituximab is usually abbreviated with the letter R and placed at the beginning or end of the chemotherapy regimen abbreviation, such as R-CHOP or CHOP-R (cyclophosphamide [Cytosan], doxorubicin/hydroxydaunorubicin [Adriamycin], vincristine [Oncovin], and prednisone [Deltasone]). Most of the chemotherapy drugs used in lymphoma treatment have been used for decades, but bendamustine (Treanda) and pralatrexate (Folotyn) were approved in the last few years, along with brentuximab vedotin (Adcetris), loncastuximab tesirine (Zynlonta) and polatuzumab vedotin (Polivy) which are monoclonal antibodies attached to a toxin.

Bendamustine (Treanda) is an alkylating agent in a class of drugs that causes damage to a cell's DNA. Pralatrexate (Folotyn) is an antimetabolite in a class of drugs that interferes with normal DNA production by eliminating folate, which is needed for the creation of DNA. Brentuximab vedotin (Adcetris) binds to the antigen (target) CD30, which is found on the cells of some forms of lymphoma and delivers the chemotherapy drug that kills cancer cells.

Brentuximab vedotin (Adcetris) is a type of antibody-drug conjugate approved for the treatment for HL and anaplastic large cell lymphoma. An antibody-drug conjugate is a monoclonal antibody that is linked to a toxin, in this case a chemotherapy agent called monomethyl auristatin E (MMAE). Loncastuximab tesirine (Zynlonta), another example of an antibody-drug conjugate, is approved to treat diffuse large B-cell lymphoma. In this case, the monoclonal antibody targets the antigen CD19 (which is expressed at the surface of some B-cell lymphomas) and is attached to an alkylating agent called

SG3199 (which kills cancer cells). Polatuzumab vedotin (Polivy), also an antibody-drug conjugate, is approved in certain patients with diffuse large B-cell lymphoma. This therapy uses the chemotherapy agent MMAE linked to a monoclonal antibody that targets CD79b, another B-cell surface protein. Each of these drugs is also being investigated for other uses.

The individual and combination chemotherapy regimens listed in Table 1 below are either currently recommended by the National Comprehensive Cancer Network or not yet approved by the U.S. Food and Drug Administration (FDA) for the treatment of lymphoma. Nearly all the progress in treating HL and NHL has been gained from information learned from clinical trials. Some of the combinations listed are used in relapsed (disease returns after treatment) or refractory (disease does not respond to treatment) lymphoma, referred to as second line therapy because they are given after frontline (initial) therapy.

HOW IS CHEMOTHERAPY GIVEN?

Most chemotherapy drugs are given orally (pill taken by mouth), intravenously (IV; injection directly into the vein), or subcutaneously (injected under the skin). A few chemotherapy drugs are injected into the space around the spinal cord, called a lumbar puncture (spinal tap). In this process, a doctor inserts a thin needle into the lower back after it has been numbed with a local anesthetic. The medications are administered one or more times a week for one or more weeks, followed by a rest period. This regular treatment schedule is called a cycle. The length of the rest period and the number of cycles vary depending on the disease and the type of drug(s) used. For more information on oral chemotherapy agents, please view the Lymphoma Research Foundation's (LRF's) Oral Agents in Lymphoma fact sheet at lymphoma.org/publications.

To make it easier to give and receive multiple cycles of IV chemotherapy into the veins, a doctor or another healthcare team member may insert or implant a central venous access device— sometimes called a catheter, port, or central line—into a large blood vessel in the patient's chest or upper extremity. The device may stay in place for a few weeks, for the duration of the chemotherapy treatment, or for several months beyond the duration of chemotherapy. Patients should discuss with their physician which type of venous access device, if any, would be best for their particular situation.

TABLE 1. CHEMOTHERAPY REGIMEN ABBREVIATIONS

REGIMENS ABBREVIATIONS	HL	NHL	MEDICATION(S)
ABVD	X*		Doxorubicin/hydroxydaunorubicin (Adriamycin, Rubex), Bleomycin (Blenoxane), Vinblastine (Velban, Velsar), Dacarbazine (DTIC-Dome)
ABVE-PC	X		Doxyrubicin (Adriamycin), Bleomycin (Blenoxane), Vinblastine (Velban, Velsar), Etoposide (Vepesid), Prednisone (Deltasone), Cyclophosphamide (Clafen, Cytoxan, Neosar)
B	X*	X	Bendamustine (Treanda)
BEACOP	X		Bleomycin (Blenoxane), Etoposide/VP16 (Etopophos, Toposar, Vepesid), Doxorubicin/hydroxydaunorubicin (Adriamycin, Rubex), Cyclophosphamide (Clafen, Cytoxan, Neosar), Vincristine (Oncovin, Vincasar PFS), Procarbazine (Matulane)
BEACOPP	X		Bleomycin (Blenoxane), Etoposide/VP16 (Etopophos, Toposar, Vepesid), Doxorubicin/hydroxydaunorubicin (Adriamycin, Rubex), Cyclophosphamide (Clafen, Cytoxan, Neosar), Vincristine (Oncovin, Vincasar PFS), Procarbazine (Matulane), Prednisone (Deltasone)
BV	X	X	Brentuximab vedotin (Adcetris)
C		X*	Cyclophosphamide (Clafen, Cytoxan, Neosar)
Chl	X	X*	Chlorambucil (Leukeran)
ChIVPP	X	X	Chlorambucil (Leukeran), Vinblastine (Velban, Velsar), Procarbazine (Matulane), Prednisone (Deltasone)
CHOP	X*	X*	Cyclophosphamide (Clafen, Cytoxan, Neosar), Doxorubicin/hydroxydaunorubicin (Adriamycin, Rubex), Vincristine (Oncovin, Vincasar PFS), Prednisone (Deltasone)
CODOXM-IVAC		X	Cyclophosphamide (Clafen, Cytoxan, Neosar), Vincristine (Oncovin, Vincasar PFS), Liposomal doxorubicin (Doxil), Cytarabine/high-dose Ara-C (Cytosar-U, Tarabine PFS), Methotrexate (Otrexup, Rheumatrex, Trexall), Ifosfamide (Ifex), Etoposide/VP16 (Etopophos, Toposar, Vepesid)
CVP (COP)	X	X*	Cyclophosphamide (Clafen, Cytoxan, Neosar), Vincristine (Oncovin, Vincasar PFS), Prednisone (Deltasone)
DHAP	X*	X*	Dexamethasone (Decadron, Dexasone), Cytarabine/high-dose Ara-C (Cytosar-U, Tarabine PFS), Cisplatin (Platinol, Platinol-AQ)
DICE	X*	X	Dexamethasone (Decadron, Dexasone), Ifosfamide (Ifex), Cisplatin (Platinol, Platinol-AQ), Etoposide/VP16 (Etopophos, Toposar, Vepesid)

*Rituximab (Rituxan) or other CD20 antibodies may be added.

REGIMENS ABBREVIATIONS	HL	NHL	MEDICATION(S)
EPOCH		X*	Etoposide/VP16 (Etopophos, Toposar, Vepesid), Prednisone (Deltasone), Vincristine (Oncovin, Vincasar PFS), Cyclophosphamide (Clafen, Cytoxan, Neosar), Doxorubicin/hydroxydaunorubicin (Adriamycin, Rubex)
ESHAP	X*	X*	Etoposide/VP16 (Etopophos, Toposar, Vepesid), Methylprednisolone (Solu-Medrol), Cytarabine/high-dose Ara-C (Cytosar-U, Tarabine PFS), Cisplatin (Platinol, Platinol-AQ)
FC		X*	Fludarabine (Fludara), Cyclophosphamide (Clafen, Cytoxan, Neosar)
FND		X*	Fludarabine (Fludara), Mitoxantrone (Novantrone), Dexamethasone (Decadron, Dexasone)
GCD	X*		Gemcitabine (Gemzar), Carboplatin (Paraplatin), Dexamethasone (Decadron, Dexasone)
GDP	X*	X*	Gemcitabine (Gemzar), Dexamethasone (Decadron, Dexasone), Cisplatin (Platinol, Platinol-AQ)
GemOX	X*	X*	Gemcitabine (Gemzar), Oxaliplatin (Eloxatin)
GVD	X*		Gemcitabine (Gemzar), Vinorelbine (Navelbine), Liposomal doxorubicin (Doxil)
HD MTX and HD Ara-C		X	High-dose methotrexate (Otrexup, Rheumatrex, Trexall), Cytarabine/high-dose Ara-C (Cytosar-U, Tarabine PFS)
HyperCVAD/MTX-Ara-C		X*	Cyclophosphamide (Clafen, Cytoxan, Neosar), Vincristine (Oncovin, Vincasar PFS), Doxorubicin/hydroxydaunorubicin (Adriamycin, Rubex), Dexamethasone (Decadron, Dexasone), Methotrexate (Otrexup, Rheumatrex, Trexall), Cytarabine/high-dose Ara-C (Cytosar-U, Tarabine PFS)
ICE	X	X*	Ifosfamide (Ifex), Carboplatin (Paraplatin), Etoposide/VP16 (Etopophos, Toposar, Vepesid)
Loncastuximab tesirine		X	Loncastuximab tesirine (Zynlonta)
MINE	X	X*	Mesna (Mesnex), Ifosfamide (Ifex), Mitoxantrone (Novantrone), Etoposide/VP16 (Etopophos, Toposar, Vepesid)
MTR		X	Methotrexate (Otrexup, Rheumatrex, Trexall), Temozolomide (Temodar), Rituximab (Rituxan)
P		X	Pralatrexate (Folotylin)
Pola-BR		X	Polatuzumab vedotin (Polivy), Bendamustine (Treanda), Rituximab (Rituxan)
SMILE		X	Methotrexate (Otrexup, Rheumatrex, Trexall), Leucovorin (Wellcovorin, Citrovorum Factor, Folinic Acid), Ifosfamide (Ifex), Mesna (Mesnex), Dexamethasone (Decadron, Dexasone), Etoposide/VP16 (Etopophos, Toposar, Vepesid), Pegaspargase (Oncaspar)
Stanford V	X		Doxorubicin/hydroxydaunorubicin (Adriamycin, Rubex), Vinblastine (Velban, Velsar), Mechlorethamine (Mustargen), Vincristine (Oncovin, Vincasar PFS), Bleomycin (Blenoxane), Etoposide/VP16 (Etopophos, Toposar, Vepesid), Prednisone (Deltasone)

*Rituximab (Rituxan) or other CD20 antibodies may be added.



WHY IS IT IMPORTANT TO ADHERE TO THE CHEMOTHERAPY TREATMENT SCHEDULE?

Patients should adhere to their chemotherapy treatment schedule because the timing of a full course of chemotherapy often works best in the treatment of their disease. In clinical studies, doctors have found that reducing the dose or delaying cycles of chemotherapy to reduce short-term side effects can decrease the treatment benefit for patients with certain types of lymphoma. Some side effects may be unpleasant but tolerable; other side effects may be more serious, but they can often be anticipated and prevented. It is very important that chemotherapy schedules be maintained to the greatest extent possible.

A healthy diet is also essential for helping a patient's body heal from both lymphoma and its treatments. A healthy diet may help

the body endure the side effects of treatment and may limit the need to modify therapy choices. Patients can speak with their healthcare team regarding these issues. For detailed information on nutrition during lymphoma treatment, view LRF's Nutrition fact sheet at lymphoma.org/publications.



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 the 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 application (app, www.FocusOnLymphoma.org) 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 program, Lymphoma Support

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Network. This program connects patients and caregivers with volunteers who have experience with lymphomas, similar treatments, or challenges, for mutual emotional support and encouragement. You may find this useful whether you or a loved one is newly diagnosed, in treatment, or in remission.

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. 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 this resource, visit our website at lymphoma.org/mobileapp, or contact the LRF Helpline at 800-500-9976 or helpline@lymphoma.org.

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 CLL/SLL including our award-winning mobile app. LRF also provides many educational activities, including our in-person meetings, webinars 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 www.lymphoma.org or contact the Helpline at (800) 500-9976 or helpline@lymphoma.org.

Supported through grants from:



The *Understanding Lymphoma* fact sheet series is published by the Lymphoma Research Foundation (LRF) for the purpose of informing and educating readers. Facts and statistics were obtained using published information, including data from the Surveillance, Epidemiology, and End Results (SEER) Program. Because each person's body and response to treatment is different, no individual should self-diagnose or embark upon any course of medical treatment without first consulting with his or her physician. The medical reviewer, the medical reviewer's institution, and LRF are not responsible for the medical care or treatment of any individual.

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Last updated 2022

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