Understanding Lymphoma and Chronic Lymphocytic Leukemia (CLL) **Chemotherapy**

Lymphoma Research Foundation

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. Chemotherapy drugs work against one of the primary characteristics of cancer cells: their ability to grow and multiply very quickly. Chemotherapy halts cell growth to prevent cancer cells from multiplying. 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 like tiredness, hair loss, infections, low blood cell counts, and loss of appetite.

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 (cells, tissues, and organs that recognize and defend the body against outside substances). 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 treatment efficacy (the ability to 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 they need to stay in the hospital (inpatient). The decision to do treatment on an inpatient basis may be made due to prolonged chemotherapy infusions, or the need to monitor for certain side effects.

For more information on chemotherapy, please view the Understanding Lymphoma and CLL Guide on the Foundation's website (visit lymphoma.org/publications).

Common Chemotherapy Regimens for Hodgkin Lymphoma (HL) and Non-Hodgkin Lymphoma (NHL)

Many chemotherapy regimens for B-cell NHL are given in combination with immunotherapy (treatments that use the body's immune system to treat cancer). This is called chemoimmunotherapy and often includes the monoclonal antibody (proteins made in the laboratory that binds to cancer cells and helps the immune system destroy them) rituximab (Rituxan). 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 [Cytoxan], doxorubicin/ hydroxydaunorubicin [Adriamycin], vincristine [Oncovin], and prednisone [Deltasone]). Another common chemotherapy is bendamustine (Treanda) and pralatrexate (Folotyn). Bendamustine (Treanda) is a chemotherapy drug which is a class of drugs that causes damage to a cell's DNA (deoxyribonucleic acid, the molecule that carries genetic information inside the cell). Pralatrexate (Folotyn) is an antimetabolite, a class of drugs that interferes with normal DNA production by eliminating folate, which is needed for the creation of DNA.

Antibody-drug conjugates (ADCs) are an exciting class of drugs that act as "biologic missiles" combining a monoclonal antibody usually with a chemotherapy agent. Brentuximab vedotin (Adcetris) is approved for the treatment for HL and anaplastic large cell lymphoma and binds to the antigen (target) CD30, which is found on the cells of some forms of lymphoma and delivers a chemotherapy drug (called MMAE, monomethyl auristatin E) that kills cancer cells. Loncastuximab tesirine (Zynlonta), is approved to treat diffuse large B-cell lymphoma (DLBCL). 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 a chemotherapy agent called SG3199. Polatuzumab vedotin (Polivy), is approved in certain patients with DLBCL. 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 of 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) lymphomas, referred to as second line therapy because they are given after frontline (initial) therapy.

Table 1: Chemotherapy Regimen Abbreviations

Regimens Abbreviations	HL	NHL	Regimens Abbreviations
ABVD	Х*		Doxorubicin/hydroxydaunorubicin (Adriamycin, Rubex), Bleomycin (Blenoxane), Vinblastine (Velban, Velsar), Dacarbazine (DTIC-Dome)
В	Х*	Х*	Bendamustine (Treanda)
BEACOPP	Х		Bleomycin (Blenoxane), Etoposide/VP16 (Etopophos, Toposar, Vepesid), Doxorubicin/ hydroxydaunorubicin (Adriamycin, Rubex), Cyclophosphamide (Clafen, Cytoxan, Neosar), Vincristine (Oncovin, Vincasar PFS), Procarbazine (Matulane), Prednisone (Deltasone)
BV	х	Х	Brentuximab vedotin (Adcetris)
С		Х*	Cyclophosphamide (Clafen, Cytoxan, Neosar)
Chl		Х*	Chlorambucil (Leukeran)
СНОР		Х*	Cyclophosphamide (Clafen, Cytoxan, Neosar), Doxorubicin/hydroxydaunorubicin (Adriamycin, Rubex), Vincristine (Oncovin, Vincasar PFS), Prednisone (Deltasone)
CODOXM-IVAC		Х	Cyclophosphamide (Clafen, Cytoxan, Neosar), Vincristine (Oncovin, Vincasar PFS), Doxorubicin/hydroxydaunorubicin (Adriamycin, Rubex) , Cytarabine/high-dose Ara-C (Cytosar-U, Tarabine PFS),Methotrexate (Otrexup, Rheumatrex, Trexall), Ifosfamide (Ifex) Etoposide/VP16 (Etopophos, Toposar, Vepesid)
CVP (COP)		Х*	Cyclophosphamide (Clafen, Cytoxan, Neosar), Vincristine (Oncovin, Vincasar PFS), Prednisone (Deltasone)
DHAP	Х	Х*	Dexamethasone (Decadron, Dexasone), Cytarabine/high-dose Ara-C (Cytosar-U, Tarabine PFS), Cisplatin (Platinol, Platinol-AQ)
EPOCH		Х*	Etoposide/VP16 (Etopophos, Toposar, Vepesid), Prednisone (Deltasone), Vincristine (Oncovin, Vincasar PFS), Cyclophosphamide (Clafen, Cytoxan, Neosar), Doxorubicin/ hydroxydaunorubicin (Adriamycin, Rubex)
ESHAP	х	Х*	Etoposide/VP16 (Etopophos, Toposar, Vepesid), Methylprednisolone (Solu-Medrol), Cytarabine/high-dose Ara-C (Cytosar-U, Tarabine PFS), Cisplatin (Platinol, Platinol-AQ)
FMC		Х*	Fludarabine (Fludara), Mitoxantrone (Novantrone), Cyclophosphamide (Clafen, Cytoxan, Neosar)
GDC	х	Х*	Gemcitabine (Gemzar), Carboplatin (Paraplatin),Dexamethasone (Decadron, Dexasone)
GDP		Χ*	Gemcitabine (Gemzar), Dexamethasone (Decadron, Dexasone), Cisplatin (Platinol, Platinol-AQ)
GemOX	х	X*	Gemcitabine (Gemzar), Oxaliplatin (Eloxatin)
GVD	х		Gemcitabine (Gemzar), Vinorelbine (Navelbine), Liposomal doxorubicin (Doxil)

Regimens Abbreviations	HL	NHL	Regimens Abbreviations
HD MTX and HD Ara-C		Х*	High-dose methotrexate (Otrexup, Rheumatrex, Trexall), Cytarabine/high-dose Ara-C (Cytosar-U, Tarabine PFS)
HyperCVAD/MTX-Ara-C		Х*	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	х	Х*	lfosfamide (Ifex), Carboplatin (Paraplatin), Etoposide/VP16 (Etopophos, Toposar, Vepesid)
Loncastuximab tesirine (Lonca-T)		Х	Loncastuximab tesirine (Zynlonta)
Pola-B		Х	Polatuzumab vedotin (Polivy), Bendamustine (Treanda)
Modified SMILE		Х	Methotrexate (Otrexup, Rheumatrex, Trexall),Ifosfamide (Ifex), Dexamethasone (Decadron, Dexasone), Etoposide/VP16 (Etopophos, Toposar, Vepesid), Pegasparginase (Oncaspar)

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

How Is Chemotherapy Given?

Most chemotherapy drugs are given orally (pill taken by mouth), intravenously (IV; injection directly into a vein), or subcutaneously (injected under the skin). A few chemotherapy drugs are injected into the space around the spinal cord, by using 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. A regular treatment schedule is called a cycle. The length of the rest period and the number of cycles vary depending on the type of lymphoma and treatment. For more information on oral chemotherapy agents, please view the Lymphoma Research Foundation'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.

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 while others may be more serious, but they can often be anticipated and prevented. It is important that chemotherapy schedules be maintained as much as 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 the Foundation'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 the Foundation's website at lymphoma.org/ publications, talk to their physician, or contact the Foundation's 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. During these visits, medical tests (such as blood tests, computed tomography [CT] scans and positron emission tomography [PET] scans) may be recommended to evaluate the need for additional treatment.

Some treatments can cause long-term side effects (occur during treatment and continue for months or years) or late side effects (appear only months, years or decades after treatment has ended). These can vary depending on the following factors:

- Duration of treatment (how long the treatment lasted)
- Frequency of treatment (how often was the treatment was administered)
- Type of treatment given
- Age and gender
- · Patient's overall health 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 (disappearance of signs and symptoms of lymphoma).

Patients and their care partners are encouraged to keep copies of all medical records. This includes 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. The Foundation's award-winning *Focus On Lymphoma* app (www.FocusOnLymphoma.org) can help patients manage this documentation.

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. The Foundation'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.

Patient Education Programs

The Foundation also offers a variety of educational activities, including live meetings and webinars for individuals looking to learn directly from lymphoma experts. These programs provide the lymphoma community with important information about the diagnosis and treatment of lymphoma, as well as information about clinical trials, research advances and how to manage/cope with the disease. These programs are designed to meet the needs of a lymphoma patient from the point of diagnosis through long-term survivorship. To view our schedule of upcoming programs, please visit lymphoma.org/programs.

Helpline

The Foundation's 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. The Foundation 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, or contact the Helpline at (800) 500-9976 or helpline@lymphoma.org.

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

Focus on Lymphoma Mobile App

Focus on Lymphoma is the first app to provide patients and their care partners 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 about this resource, visit our website at lymphoma.org/mobileapp, or contact the Foundation's Helpline at (800) 500-9976 or helpline@lymphoma.org. Lymphoma

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