TREATMENT UPDATE:

Diffuse Large B-Cell Lymphoma (DLBCL)

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Treatment Update: Diffuse Large B-Cell Lymphoma (DLBCL)

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All people depicted in the photographs in this booklet are models, used for illustrative purposes only.

Diffuse large B-cell lymphoma (DLBCL) is a cancer that starts in white blood cells called lymphocytes. More than 18,000 people in the United States are diagnosed with DLBCL each year.

There are two types of lymphoma: Hodgkin's and non-Hodgkin's. DLBCL is the most common type of non-Hodgkin's lymphoma. In about 60 percent of cases, DLBCL grows in the lymph nodes, small bean-shaped organs located throughout the body that remove waste and fluids and help fight infection. DLBCL that develops in a place other than the lymph nodes is called "extranodal." The most common places where extranodal DLBCL develops are the stomach and gastrointestinal tract. There are two major subtypes of DLBCL: germinal center B-cell (GCB) and activated B-cell (ABC).

Diagnosis and Staging

The first sign of DLBCL is often a painless, quickly-growing mass (lump) in the neck, groin or abdomen. If DLBCL is suspected, a biopsy is performed, in which all or part of the mass is removed surgically and examined under a microscope. If a diagnosis of DLBCL is confirmed, further tests are performed to "stage" the cancer. Stages of DLBCL are defined as follows:

- **Stage I.** The cancer is in only one lymph node region, lymph structure or other site.
- **Stage II.** The cancer is in two or more lymph node regions or structures on one side of the diaphragm (the large muscle that separates the belly from the chest).
- **Stage III.** The cancer is in lymph node regions or structures on both sides of the diaphragm.
- **Stage IV.** The cancer has spread to other tissues and organs, which may include the liver, lungs or bone marrow.

As DLBCL can advance quickly, it usually requires immediate treatment once diagnosed.

Treatment Options

Chemotherapy-based approaches

The standard of care for newly-diagnosed DLBCL is a regimen called R-CHOP: rituximab (Rituxan), cyclophosphamide (Cytoxan), doxorubicin (Adriamycin), vincristine (Oncovin) and prednisone. Rituximab is a monoclonal antibody, a lab-generated protein that helps the immune system recognize and destroy cancer cells. Cyclophosphamide, doxorubicin and vincristine are chemotherapies. Prednisone is a steroid.

In stage III or IV DLBCL, the R-CHOP regimen is usually given once every 21 days over the course of 6-8 cycles. The drugs, except for the prednisone, are given as an infusion. The prednisone is given orally. Fewer cycles (3-4) may be used in the treatment of localized (stage I or II) DLBCL. Sometimes the chemotherapy etoposide (Etopophos, Vepesid) is added to the R-CHOP regimen. If this is the case, the regimen is called R-CHOEP.

A related regimen, R-EPOCH, is the use of the same drugs administered as a continuous infusion over the course of 4 days. The treatment is repeated every 21 days over the course of several cycles as determined by the person's individual circumstances.

Additionally, the monoclonal antibody rituximab/hyaluronidase human (Rituxan Hycela) can be given as an initial treatment for DLBCL, in combination with R-CHOP or R-CHOEP. It is given as a subcutaneous (beneath the skin) injection.

Radiation therapy

In addition to chemotherapy-based regimens, "external beam" radiation therapy is typically used to treat localized DLBCL. This form of radiation therapy uses a machine outside of the body to generate a radiation beam. It is typically given five days per week for 3-4 weeks.

CAR T-Cell Therapy

Chimeric antigen receptor (CAR) T-cell therapy is a type of immunotherapy that uses a person's own T-cells (a type of white blood cell) to treat certain types of relapsed (recurred) or refractory (not responding to treatment) lymphomas, including DLBCL.

The CAR T-cell therapies approved by the U.S. Food and Drug Administration (FDA) for DLBCL are axicabtagene ciloleucel (Yescarta), lisocabtagene maraleucel (Breyanzi) and tisagenlecleucel (Kymriah).

Based on a person's specific situation, CAR T-cell therapy may be conducted on an outpatient basis or require a hospital admission. The process is similar regardless of the drug used or the specific subtype of DLBCL:

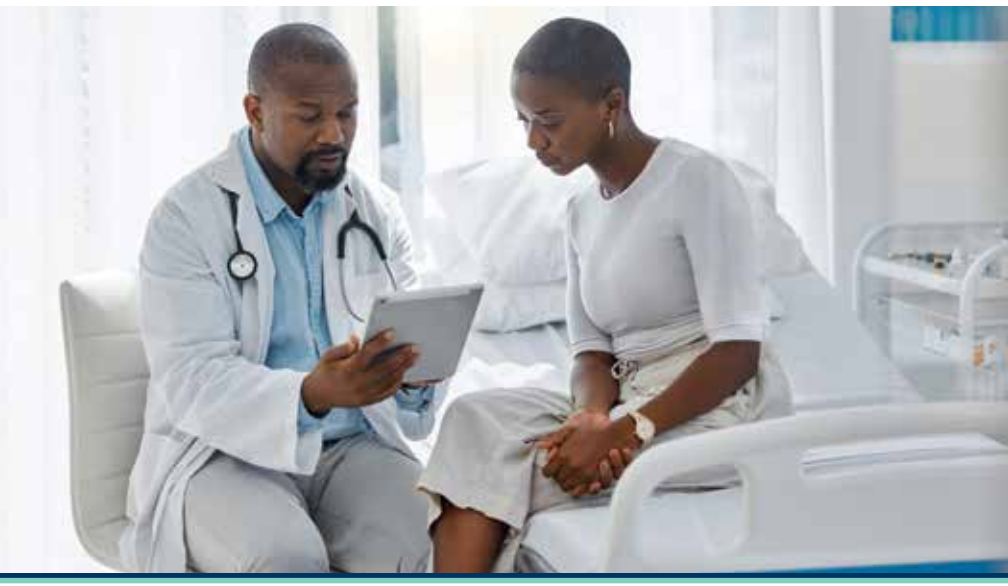
- Blood is drawn from the patient via an intravenous catheter (a flexible tube).
- T-cells are isolated from the rest of the blood.
- In a laboratory, the T-cells are genetically re-engineered by adding a chimeric antigen receptor to their surface.
- The modified T-cells (which are now CAR T-cells) are expanded to number in the hundreds of millions.
- The CAR T-cells are infused back into the patient where they target and destroy cancer cells.

Recently approved therapies

In April 2023, the U.S. Food and Drug Administration (FDA) approved the combination of polatuzumab vedotin (Polivy) and R-CHOP as a treatment for patients with previously untreated DLBCL. Polatuzumab vedotin, an antibody-drug conjugate, works by combining a chemotherapy with an antibody that seeks out cancer cells.

In May 2023, the FDA granted accelerated approval to epcoritamab-bysp (Epkinly), for relapsed or refractory DLBCL after treatment with two or more lines of systemic therapy. Epcoritamab-bysp is a targeted therapy given as a subcutaneous (under the skin) injection.

In June 2023, the FDA granted accelerated approval to glofitamab-gxbm (Columvi) for relapsed or refractory DLBCL after treatment with two or more lines of systemic therapy. A targeted therapy, glofitamab-gxbm is given intravenously (through a needle or tube into a vein).



The Importance of Clinical Trials

Clinical trials are the standard by which we measure the worth of new treatments and the quality of life of patients as they receive those treatments. For this reason, doctors and researchers urge people with cancer to take part in clinical trials.

Your doctor can guide you in making a decision about whether a clinical trial is right for you. Here are a few things that you should know:

- Often, people who take part in clinical trials gain access to and benefit from new treatments.
- Before you participate in a clinical trial, you will be fully informed as to the risks and benefits of the trial, including any possible side effects.
- Most clinical trials are designed to test a new treatment against a standard treatment to find out whether the new treatment has any added benefit.
- You can stop taking part in a clinical trial at any time for any reason.

Treatment-Specific Side Effects

All cancer treatments can cause side effects. It's important that you report any side effects that you experience to your health care team so they can help you manage them. Report them right away—don't wait for your next appointment. Doing so will improve your quality of life and allow you to stick with your treatment plan. It's important to remember that not all people experience all side effects, and people may experience side effects not listed here.

Chemotherapy-based treatment

- Hair loss
- Increased risk of infection (from having too few white blood cells)
- Anemia (low number of red blood cells)
- Easy bruising or bleeding
- Peripheral neuropathy (numbness or tingling in hands and feet)

Radiation therapy

The side effects of radiation therapy can include dryness, swelling, peeling, redness and (rarely) blistering. If a reaction occurs, contact your health care team so the appropriate treatment can be prescribed. It's especially important to contact your health care team if there is any open skin or painful area, as this could indicate an infection. Infections can be treated with an oral antibiotic or topical antibiotic cream.

CAR T-Cell Therapy

Immunotherapy, including CAR T-cell therapy, travels through the bloodstream to help prompt what is called an "immune response." Because immunotherapy can affect healthy cells as well as cancer cells, certain side effects may be experienced. The potential side effects associated with CAR T-cell therapy include:

- **Cytokine-Release Syndrome (CRS).** The infusion of CAR T-cells into the body results in the production of large numbers of cytokines (molecules that help cells communicate), which can cause the immune system to become excessively active. This can lead to CRS, with symptoms such as high fever and flu-like symptoms. These side effects can be controlled and reversed with cytokine-blocking drugs and steroids.
- **B-Cell Aplasia.** The FDA-approved CAR T-cell therapies destroy normal as well as cancerous B-cells, which can cause B-cell aplasia (low numbers of B-cells), in which the body is less able to make the antibodies that protect against infection. Immunoglobulin replacement, administered intravenously, can be used to treat or prevent infection.
- **Tumor Lysis Syndrome (TLS).** When cancer cells break down (are destroyed) very quickly, they release large amounts of potassium, phosphate and uric acid into the blood. This can result in TLS, a group of conditions that can cause neurological, heart or kidney problems. TLS is managed by medicines that decrease potassium and uric acid levels in the blood. Medicines may also be prescribed that help increase urination.
- **Changes in cognition.** Some changes in cognition (thought processes) ranging from mild to severe can occur within several days of CAR T-cell therapy. The symptoms are often treated with steroids and are almost always reversible.

Because of these potential side effects, people who undergo CAR T-cell therapy should stay close to their treatment location for at least four weeks, so they can be closely monitored by their healthcare team.

Side Effects of Targeted Therapy

Targeted therapy doesn't have the same effect on the body as do chemotherapy drugs, but it can still cause side effects. Side effects of targeted therapies can include diarrhea, liver problems (such as hepatitis and elevated liver enzymes), nerve damage, high blood pressure and problems with blood clotting and wound healing.

General Side Effects

Some side effects may occur across treatment approaches. Following is guidance on how to manage these side effects should they occur.

Managing Digestive Tract Symptoms

Nausea and vomiting

- Avoid food with strong odors, as well as overly sweet, greasy, fried or highly seasoned food.
- Eat meals that are chilled, which often makes food more easily tolerated.
- Nibble on dry crackers or toast. These bland foods are easy on the stomach.
- Having something in your stomach when you take medication may help ease nausea.

Diarrhea

- Drink plenty of water. Ask your doctor about using drinks such as Gatorade which provide electrolytes. Electrolytes are body salts that must stay in balance for cells to work properly.
- Over-the-counter medicines such as loperamide (Imodium A-D and others) and prescription drugs are available for diarrhea but should be used only if necessary. If the diarrhea is bad enough that you need medicine, discuss it with your doctor or nurse.
- Choose fiber-dense foods such as whole grains, fruits and vegetables, all of which help form stools.
- Avoid food high in refined sugar and those sweetened with sugar alcohols such as sorbitol and mannitol.

Managing loss of appetite

- Eating small meals throughout the day is an easy way to take in more protein and calories, which will help maintain your weight. Try to include protein in every meal.
- To keep from feeling full early, avoid liquids with meals or take only small sips (unless you need liquids to help swallow). Drink most of your liquids between meals.
- Keep high-calorie, high-protein snacks on hand such as hard-boiled eggs, peanut butter, cheese, ice cream, granola bars, liquid nutritional supplements, puddings, nuts, canned tuna or trail mix.
- If you are struggling to maintain your appetite, talk to your health care team about whether appetite-building medication could be right for you.

Managing Fatigue

Fatigue (extreme tiredness not helped by sleep) is one of the most common side effects of many cancer treatments. If you are taking a medication, your doctor may lower the dose of the drug, as long as it does not make the treatment less effective. If you are experiencing fatigue, talk to your doctor about whether taking a smaller dose is right for you.

There are a number of other tips for reducing fatigue:

- Take several short naps or breaks during the day.
- Take short walks or do some light exercise, if possible.
- Try easier or shorter versions of the activities you enjoy.
- Ask your family or friends to help you with tasks you find difficult or tiring.
- Save your energy for things you find most important.

Fatigue can be a symptom of other illnesses, such as anemia, diabetes, heart disease, rheumatoid arthritis and depression. So be sure to ask your doctor if they think any of these conditions may be contributing to your fatigue.

Managing Pain

To help your doctor prescribe the best medication, it's useful to give an accurate report of your pain. Keep a journal that includes information on:

- Where the pain occurs
- When the pain occurs
- How long it lasts
- How strong it is on a scale of 1 to 10, with 1 being the least amount of pain and 10 the most intense
- What makes the pain feel better and what makes it feel more intense

There are a number of options for pain relief, including prescription and over-the-counter medications. It's important to talk to a member of your health care team before taking any over-the-counter medication to determine if they are safe and will not interfere with your treatments.

Physical therapy, acupuncture and massage may also be of help in managing your pain. Consult with a member of your health care team before beginning any of these activities.

Communicating With Your Health Care Team

As you manage your DLBCL, it's important to remember that you are a consumer of health care. The best way to make decisions about health care is to educate yourself about your diagnosis and get to know the members of your health care team, including doctors, nurse practitioners, physician assistants, nurses, dietitians, social workers and patient navigators.

Here are some tips for improving communication with your health care team:

Start a health care journal. Having a health care journal or notebook (either on paper or in a digital format) will allow you to keep all of your health information in one place. You may want to write down the names and contact information of the members of your health care team, as well as any questions for your doctor.

Prepare a list of questions. Before your next medical appointment, write down your questions and concerns. Because your doctor may have limited time, ask your most important questions first and be as specific as possible.

Bring someone with you to your appointments or have them be present during telehealth sessions. Even if you have a journal and a prepared list of questions or concerns, it's always helpful to have support when you go to your appointments. The person you bring may also think of questions to ask your doctor or remember details about your symptoms or treatment that you may have forgotten.

Write down your doctor's answers. Taking notes will help you remember your doctor's responses, advice and instructions. You can also ask the person who accompanies you to take notes for you. If you have a mobile device, ask if you can use it to take notes. Keeping notes will help you review the information later.

Record your visit if your doctor allows it. Recording the conversation with your doctor gives you a chance to hear specific information again or share it with family members or friends.

Incorporate other health care professionals into your team. Your oncologist is an essential member of your health care team, but there are other health care professionals who can help you manage your diagnosis and treatment:

- Your primary care physician should be kept updated about your DLBCL treatment and any test results.
- Your local pharmacist is a great source of knowledge about the medications you are taking. Have all of your prescriptions filled at the same pharmacy to avoid the possibility of harmful drug interactions.
- Make sure your oncologist knows of any other medical conditions you have or any pain you are experiencing so that they can consult with your primary care physician or specialists as needed.

Remember, there is no such thing as over-communication.

Cancer*Care*'s Free Support Services and Programs

It can be very difficult to receive a diagnosis of DLBCL, and adjusting to the necessary changes in your life can be challenging.

Cancer*Care*® can help. We are a national nonprofit organization providing free, professional services to anyone affected by cancer. Our licensed oncology social workers can provide support and education, help in navigating the complicated health care system and offer information on support groups and other resources.

To learn more about how Cancer*Care* helps, call us at 800-813-HOPE (4673) or visit www.cancercare.org.

You will likely also build your own personal support network composed of family and friends. In doing so, it's best to take some time to think about the people in your life and how they are best suited to help. Match the task to their strengths—ask a family member who loves to shop to pick up something for you at the store, or ask a friend who's a good listener to come over for a chat.

Frequently Asked Questions

Q: What treatment approaches for DLBCL are currently being studied?

A: There is a great deal of research being conducted for the treatment of DLBCL; for example:

- Results from a phase II clinical trial showed that the ABC subtype of relapsed or refractory DLBCL was more responsive to the targeted therapy ibrutinib (Imbruvica) than was the GCB subtype. This is important, as the ABC subtype is less likely to respond to standard R-CHOP treatment. Based on these results, an international phase III trial is underway comparing standard chemotherapy with or without ibrutinib in patients with non-GCB subtypes of DLBCL.
- Other research is exploring the addition of lenalidomide (Revlimid) to R-CHOP chemotherapy. The results to date seem to indicate show that this regimen may work better in the ABC subtype of DLBCL.

Q: Who is most likely to develop DLBCL?

A: Although DLBCL can develop in all age groups, it is most commonly found in middle-aged or older adults. Men are slightly more likely to develop DLBCL than women and it is more common in white people than in those of Asian or African descent. As DLBCL is not an inherited disease, family members of those with DLBCL are not at substantially increased risk of developing DLBCL.

Q: What is a treatment summary and why is it important?

A: Keeping your own records up-to-date in the form of a treatment summary can be helpful, as it allows you and your family members to have instant access to the specifics of your thyroid cancer diagnosis and treatment. A treatment summary should include:

- Your name and date of birth
- Date of diagnosis
- Prescribed therapy/therapies, including dates started and stopped and dosages when appropriate
- Dates and types of baseline and post-diagnosis testing and the results of these tests
- Other medications and supplements you are taking
- Names, affiliations and contact information of all members of your health care team

Ask the members of your health care team what they suggest be included. Take your personal record with you when you visit any doctor, not just your oncologist.

Resources

CancerCare®
800-813-HOPE (800-813-4673)
www.cancercare.org

American Cancer Society
800-227-2345
www.cancer.org

Cancer.Net
Patient information from the American Society of Clinical Oncology
888-651-3038
www.cancer.net

National Cancer Institute
800-422-6237
www.cancer.gov

CLINICAL TRIALS WEBSITES

ClinicalTrials.gov
www.clinicaltrials.gov

EmergingMed
www.emergingmed.com

National Cancer Institute
www.cancer.gov

Cancer Support Community
888-793-9355
www.cancersupportcommunity.org

National Coalition for Cancer Survivorship
877-622-7937
www.canceradvocacy.org

Lymphoma Coalition
www.lymphomacoalition.org

Lymphoma Research Foundation
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