Understanding
Large B-Cell Lymphoma

A Patient-Friendly Guideline

(Based on EHA Medical Guidelines)

Table of contents

Introductory Sections

What is lymphoma?

Lymphoma is the most commonly occurring blood cancer.
One million people around the world are living with lymphoma today, yet many people are still unaware of lymphoma and that it can be a life-threatening form of cancer.1
You are reading this because you or someone you care about has been recommended treatment following a diagnosis of large B-cell lymphoma (LBCL), which is an aggressive type of lymphoma.

What is the purpose of this patient guideline?

Many of the available clinical practice guidelines are intended for healthcare professionals, and, while these can be valuable to many patients and their loved ones, they can be overwhelming for some ***(See Figure 1: An example of a current clinical practice guideline for the diagnosis, treatment, and follow-up of LBCL).***

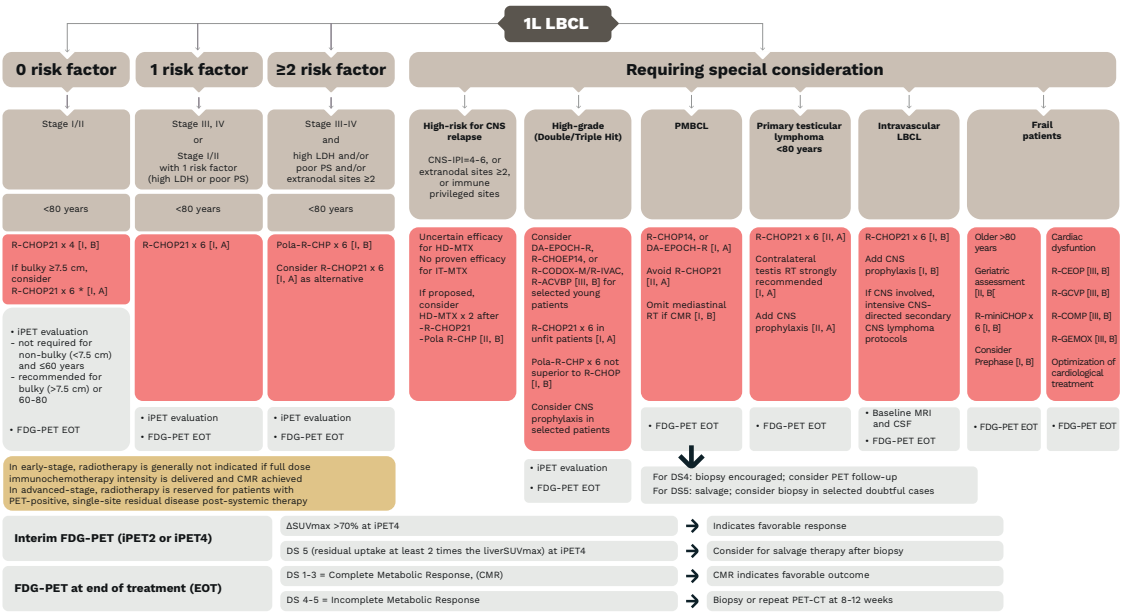

Figure 1: An example of a current clinical practice guideline for the diagnosis, treatment, and follow-up of LBCL.2

Thieblemont C, et al. B-cell lymphoma (LBCL): EHA Clinical Practice Guidelines for diagnosis, treatment, and follow-up. Hemasphere. 2025;9:e70207.

Introduction

"Clinical practice guidelines are intended for healthcare professionals, and, while these can be valuable to many patients and their loved ones, they can be overwhelming for some."

This patient guideline comprises four key patient-focused sections (below), and is supported by a glossary, which will help you understand the terminology surrounding LBCL, and a list of trusted support organisations, including local/regional options:

Section 1. **What are my goals of treatment?**

Section 2. **What is considered when deciding on treatment?**

Section 3. **What are my treatment options?**

Section 4. **What happens after my treatment is finished?**

This guideline is not a substitute for medical advice, and any care decisions should be made following professional advice and in collaboration with your lymphoma care team.
This patient guideline, guided by experts within Lymphoma Coalition and prepared in conjunction with The European Hematology Association (EHA), is written with you in mind – its aim is to bring clarity to the treatment pathway. It will provide you with the key information that you will need to understand and follow the path of treatment for LBCL, serving as a reference document throughout the treatment journey. The aim is to provide a plain-language overview of the treatment pathway for LBCL. In addition, we will direct you to other reliable sources of information on LBCL. Taken together, the information available will provide you with a framework for further conversation with your care providers.

What is Lymphoma Coalition?

Lymphoma Coalition is a non-profit organisation comprising a world-wide network of patient advocacy groups that support those affected by lymphoma. Lymphoma Coalition is the leading global coalition of patient organisations; we work together to generate and provide trusted information, knowledge, and best practice to influence and make possible equitable care.

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Lymphoma Coalition achieves these goals by engaging individuals with lymphoma and their caregivers in all aspects of their care. Support is tailored with the understanding that every patient is unique with a different set of complex needs that may change over time. It is important to listen to and hear the patient with lymphoma and those close to them, so that the focus of their care and needs are included throughout the decision-making process, respecting their culture, input, dignity, intelligence, and capacity to make informed decisions about the impact on their lives and their care. Lymphoma Coalition prioritises including patient organisations as active partners representing a patient's emotional and psychosocial needs at every stage of care, including treatment and protocol development. Lastly, what we learn is used to inform research throughout the clinical and treatment development continuum.

The goal of Lymphoma Coalition is to build a better future for everyone affected by lymphoma. For more information, visit the Lymphoma Coalition website at https://lymphomacoalition.org/.

About Lymphoma Coalition member organisations

At the heart of Lymphoma Coalition is a diverse community of over 100 member organisations spanning more than 55 countries, a truly global alliance of patient advocates and dedicated non-profits working across every continent to champion the needs of the lymphoma and chronic lymphocytic leukaemia (CLL) community. By uniting these global voices, Lymphoma Coalition provides a platform for collaboration, capacity building, and the sharing of current research, ensuring that no patient has to face lymphoma or CLL alone.
To learn more about where you can find a member organisation close to you, please visit: https://lymphomacoalition.org/member-organisation/

What is European Hematology Association (EHA)?

The European Hematology Association (EHA) is a leading force in hematology, bringing the community together to share knowledge, collaborate, connect, and grow. Together, we accelerate progress through education, science, and innovation. We improve patient outcomes and help move closer to curative outcomes—across Europe and beyond.

EHA develops comprehensive, evidence-based clinical practice guidelines to support healthcare professionals in the diagnosis, treatment, and management of hematologic diseases. Launched through the EHA Guidelines Committee in 2019, this initiative follows a rigorous methodology to ensure high-quality and standardized recommendations covering both benign and malignant blood disorders.

These guidelines are developed through systematic evidence reviews as well as expert consensus and address a wide range of conditions such as leukemia, lymphoma, myeloma, anemia, bone marrow failure syndromes, and bleeding disorders. They offer clinicians structured diagnostic pathways, treatment algorithms, and follow-up strategies based on the current scientific data.

Importantly, patient representatives are included in every EHA Guideline project. Their role is to review the manuscript, provide comments, and contribute with the patient's perspective, ensuring recommendations reflect real-world needs, values, and priorities of those living with hematologic conditions. This strengthens the relevance, clarity, and applicability of every guideline.

EHA also works closely with leading international societies to co-develop or endorse guidelines aligned with the latest scientific evidence and clinical best practices. By integrating interdisciplinary expertise, patient insights, and continuous updates, EHA Guidelines serve as a trusted, authoritative resource that elevates the standard of care in hematology across Europe and beyond.

For more information, visit Clinical practice - The European Hematology Association (EHA) website: https://ehaweb.org/clinical-practice

SECTION **1.**

WHAT ARE MY GOALS OF TREATMENT?

Depending on the individual, the goal(s) of treatment may be to either achieve long-term remission of your cancer, prolong life and improve life expectancy (sometimes referred to as **overall survival**), allowing you to lead as normal a life as possible for as long as possible, or to improve quality of life. These goals are not mutually exclusive, but the balance between them may change over time. While there are established protocols for the treatment of LBCL, the treatment journey itself is highly individual and based on well-established disease- and patient-specific factors.

It is important to understand that your treatment course may differ from others with a similar diagnosis. This is a strength of modern cancer care and means that the treatment you are being offered is based on both the highest level of medical knowledge and recommendation, and according to your own unique diagnosis and clinical condition or **comorbidities**.

Many patients can be cured with **first-line** treatment, and studies show that patients with diffuse LBCL, a common subtype of LBCL, who are lymphoma-free at 2 years after diagnosis have an identical overall survival to that of the general population, while those with LBCL overall have comparable overall survival.3

However, it is important to understand that your individual treatment goals will be guided by a number of disease- and patient-specific factors, will differ according to your individual risk profile, and should always be determined in collaboration with your care team.

SECTION **2.**

WHAT IS CONSIDERED WHEN DECIDING ON TREATMENT?

A number of disease- and patient-specific factors can influence the type of treatment recommended to an individual patient, including patient age, current state of health, the specific nature of the diagnosis, and the likelihood of experiencing any adverse events (sometimes known as 'side effects') that maybe associated with specific therapies.

In this section we will guide you through the factors that can influence your treatment choices, discuss the common steps in the treatment pathway, and introduce some of the more common concerns you may experience when undergoing treatment for LBCL.

2.1 What is my diagnosis and what does it mean in terms of prognosis and treatment options?

2.1.1 Lymphoma

Lymphoma is cancer of the **lymphocytes**, which are the white blood cells that help to fight infection. Lymphocytes are found in a liquid called lymph, which travels throughout our bodies in the lymphatic system, a series of vessels, nodes, and organs such as the spleen, bone marrow, and thymus that are part of our immune system. Lymphocytes often gather in the lymph nodes to fight infection. While you can feel the lymph nodes in your armpits, neck and groin, they can be found in almost any part of the body.

There are different types of lymphocytes, including **B lymphocytes** (also called B cells) and **T lymphocytes** (also called T cells). They are both important to your immune system, but they have different roles.

2.1.2 Large B-cell lymphoma

Large B-cell lymphoma, or LBCL, represent a specific group of ~20 lymphoma types. LBCLs account for approximately one-third of all lymphomas in adults.4 LBCLs are characterised by large, abnormal B lymphocytes.

In Europe, the incidence rate for LBCL is ~28,000 cases per year,5 with more males being affected when compared to females.4

SECTION **2.**

In most patients, the aetiology (underlying cause) of LBCL remains unclear. However, various risk factors for the development of LBCL such as immunodeficiency (an immune system that doesn't work properly), B-cell activating autoimmune diseases, virus infections, or a family history of lymphoma have been identified.6 Having one or more risk factors can increase the chance of developing an LBCL, but risk factors alone don't cause lymphoma.

"You are reading this because you, or someone you care about, has been diagnosed with a large B-cell lymphoma."

2.1.3 Diffuse LBCL

Diffuse large B-cell lymphoma (DLBCL) is the most common type of LBCL, and accounts for approximately one-third of all lymphomas in adults.4

DLBCL is often an aggressive or fast-growing lymphoma. It can occur in the lymph nodes ('nodal disease') or outside of the lymphatic system in the gastrointestinal tract, testes, thyroid, skin, breast, bone, or brain ('extranodal disease'). Extranodal disease usually indicates a more advanced stage of lymphoma.

DLBCL can present as a new diagnosis (de novo disease) or as a histological transformation of another clinically indolent low-grade B-cell lymphomas like follicular or chronic lymphocytic leukaemia/small lymphocytic lymphoma; de novo DLBCL cases have better prognoses than histologically transformed cases.

DLBCL exists as several subtypes, with the specific subtype at diagnosis influencing the path of treatment. Subtypes are grouped mainly by the type of cells from which the cancer originates. Activated B-cell-like DLBCL and germinal centre B-cell-like DLBCL represent the two most common molecular subtypes. Less common subtypes of DLBCL include primary cutaneous DLBCL, leg type, Epstein-Barr Virus (EBV)-positive DLBCL NOS, DLBCL associated with chronic inflammation, fibrin-associated DLBCL, primary DLBCL of the central nervous system (CNS), DLBCL arising from follicular or mantle cell lymphoma (transformed), and Richter's transformation (DLBCL arising from chronic lymphocytic leukaemia).

SECTION **2.**

2.1.4 Other LBCL (sub)types

Other types of LBCL include follicular lymphoma, grade 3B; high-grade B-cell lymphoma (HGBL: HGBL-not otherwise specified (NOS), HGBL with MYC and BCL6 rearrangements (ICC), and HGBL with 11q aberration); mediastinal gray zone lymphoma (MGZL), primary mediastinal large B-cell lymphoma (PMBL), ALK-positive LBCL, intravascular LBCL, T-cell/histiocyte-rich LBCL, LBCL with 11q aberration, and LBCL with IRF4/MUM1 rearrangement.

If you have been diagnosed with a less common subtype of LBCL your physician will likely invite you to discuss your treatment options in more detail as the approach taken at diagnosis may differ from what is done for more common types.

2.2 What factors will influence choice of treatment?

Personal treatment plans (and goals) will be influenced by numerous factors including age, general health, and your medical history. You should also tell your physician if you are planning on becoming pregnant, as some cancer treatments can affect fertility.
In addition to these patient-specific factors, the specific nature of the diagnosis will be used to guide treatment. This will be discussed in more depth later in this document, in the Section 3.4 entitled **Treatment protocols according to LBCL (sub)type and patient profile**.

2.2.1 Medical history

Medical history is a record of all health issues and treatment through the life of an individual patient. This can include other current diseases or medical conditions (called comorbidities) or those experienced by the patient in the past. You should be prepared to list any current or historical illness or injury and when it happened and mention any symptoms you are currently experiencing.

"Bring a list of old and new medicines and any over-the-counter medicines, herbal treatments, or supplements you take, as some may interact with or affect lymphoma treatment."

2.2.2 Medications

Bring a list of old and new medicines and any over-the-counter medicines, herbal treatments, or supplements you take, as some may interact with or affect LBCL treatment. Note that certain commonly used supplements, including natural products such as turmeric/curcumin, ginkgo biloba, green tea extract, St John's Wort, and high-dose antioxidant supplements, etc., can interfere with lymphoma treatment. Tell your doctor if you take any herbal or natural products so they can check for potential interactions.

2.2.3 Family history, future plans

You will also be asked about the medical/health history of family members, and whether there is a family history of heart disease, cancer, and/or diabetes. If there is a family history of cancer, it is important to know the specific type of cancer (or the location of the cancer), if it is/was in multiple locations, and whether molecular/genetic testing was undertaken.

2.2.4 Fracture-risk assessment

The risk of osteoporotic bone fractures (often called fragility fractures, a bone break that occurs because the bone has become weak and brittle due to osteoporosis) is higher in patients with LBCL. In addition, certain health conditions (osteoporosis, osteopenia, prior fracture, and rheumatoid arthritis), bone involvement with lymphoma, and corticosteroid therapy are independent risk factors. Your doctor may want to do a baseline osteoporosis risk, likely using the FRAX® assessment for osteoporosis risk,7 before beginning treatment.
Patients receiving steroid therapy have been shown to benefit from vitamin D treatment in other contexts, so this may be recommended by your doctor.

2.2.5 Lifestyle

Since general health and level of fitness will be taken into consideration when making treatment decisions, your care team will advise smoking cessation (if applicable). This is essential for all patients undergoing treatment for LBCL. If smoking cessation counselling is required, this should be discussed with your care team.

In addition to smoking cessation, exercise and the food you eat are an important element of lymphoma care. Scientific evidence has shown lifestyle changes, such as physical activity and a healthy diet, can be valuable to help patients manage fatigue, improve heart and lung health, and support long-term recovery.[8]

2.2.6 Special considerations in older patients

It is important to note that LBCL incidence (the number of people diagnosed) increases with age, and that age can influence treatment decisions. As such, older patients will be offered what is referred to in the medical community as a 'geriatric assessment', a special series of tests to see how well they are functioning physically, mentally, and emotionally – all of which naturally decline as people age.

These assessments, directed towards mature patients, help identify candidates who can tolerate curative treatments versus those needing different treatment approaches that are less harsh, or palliative care. This approach is a scientifically proven method to ensure appropriate, patient-specific care with a focus on quality of life. In addition, in older patients, 'Goals of care' discussions with patients and families that include palliative options, where appropriate, may be instigated by the care team.

2.3 What tests are needed and how often will these be repeated?

A number of different tests are used to make sure the diagnosis is correct, to know how much lymphoma is in the body (called **'staging'**), to help doctors make an assessment of how well different treatments might work, and to measure if treatments are working.

The patient will likely be recommended a range of tests that include a physical assessment, a procedure to obtain a biopsy for laboratory assessment, and imaging; in addition, there may be additional tests in older patients, as discussed previously.

See Table 1 (next page): Investigations/procedures for LBCL diagnosis, staging, and prognostic-risk assessment for an overview of the more common procedures and tests performed in a patient diagnosed with an LBCL.

TABLE **1** INVESTIGATIONS/PROCEDURES FOR LBCL DIAGNOSIS, STAGING, AND PROGNOSTIC-RISK ASSESSMENT

Table 1 *shows the baseline investigations for LBCL diagnosis, staging, and future-risk assessments with the highest level of recommendation based on treatment guidelines and clinical studies. You will likely be recommended many of these tests at diagnosis, with some being recommended again if your disease returns and to determine suitability for further treatment. Other tests are available and may be recommended on the basis of disease- or patient-specific factors.*

INVESTIGATION/PROCEDURE	NOTES
Surgical excision biopsy	Preferred method for obtaining a sample
Diagnosis by specialised hematopathology laboratory (a laboratory that has experience in studying blood diseases or disorders and in diagnosing and profiling lymphomas)	Includes molecular/genetic tests to determine the specific type of lymphoma in a patient
Positron emission tomography–computed tomography (PET-CT)	Preferred method for staging
Blood tests	Used to check your overall health, check your blood cell counts, show if you have other medical conditions, and how well your kidneys and liver are functioning
Central nervous system (CNS) assessment: • **Magnetic resonance imaging (MRI)** of the brain/spine • Cerebrospinal fluid (CSF) assessment performed on a sample obtained by lumbar puncture (a 'spinal tap'; cytology and immunophenotyping)	Used to see if the lymphoma has spread to your central nervous system

TABLE **1** INVESTIGATIONS/PROCEDURES FOR LBCL DIAGNOSIS, STAGING, AND PROGNOSTIC-RISK ASSESSMENT

INVESTIGATION/PROCEDURE	NOTES
Heart function (cardiac) assessment; tests may include: • Electrocardiogram (ECG) • Ultrasound • Echocardiogram • Blood-pressure measurement	Performed at diagnosis for all patients before treatment with certain types of **chemotherapy**, CAR-T cells, or **bispecific antibodies**
Performance and prognostic scores: • Eastern Cooperative Oncology Group (ECOG) **performance status** • International Prognostic Index (IPI) • Central nervous system-International Prognostic Index (CNS-IPI score)	Performed at diagnosis The ECOG performance status evaluates the patient's ability to care for themself, daily activity, and physical ability The IPI considers the patient's ECOG score, their age, the stage of the lymphoma (the parts of the body and a blood test that can show tissue damage from an injury, disease or infection (serum LDH) Can be used to guide treatment
Molecular and genetic testing: • Fluorescence in situ hybridization (FISH) for genetic alterations in MYC genes • FISH for BCL2 and BCL6 genes (if MYC+ identified)	Genetic profiling at diagnosis Can be used to guide treatment and/or as a prognostic tool to determine likely outcomes
FRAX® assessment for osteoporosis risk	The risk of osteoporotic bone fractures is higher in the LBCL patient population

Based on the Large B-cell lymphoma (LBCL): EHA Clinical Practice Guidelines for diagnosis, treatment, and follow-up.[2]

SECTION **2.**

2.3.1 Physical examination

A physical examination is recommended for all new patients and includes the following elements:[9]

- Temperature, blood pressure, pulse, breathing rate
- Height/weight
- Physical examination to see if parts of your body and organs are of normal size, are soft or hard, or sensitive to touch
- Physical examination for enlarged lymph nodes in the neck, underarm, and groin

Physical examination may be repeated at different stages of your treatment journey, and include re-checking of lymph nodes, liver, spleen, etc., with the aim of looking for new swelling, tenderness, infections, or possible adverse effects of treatment, or to compare to previous examinations to assess response to therapy (for example, shrinking lymph nodes would represent a positive response to treatment)

2.3.2 Biopsy and imaging

Following a diagnosis (or suspected diagnosis) of an LBCL, patients will be recommended for biopsy, which is the removal of a piece of the suspected lymphoma (the specimen). This may be done through an incision or by using a special type of needle. The specimen will be sent to a specialised laboratory with expertise in diagnosing and profiling lymphoma.

The specimen will be tested in accordance with treatment and diagnostic guidelines, which are based on recommendations made by the World Health Organization.2 These tests help determine the subtype of lymphoma you have and anything specific your doctor/care team should know about your lymphoma.

Guideline recommendations include molecular/genetic testing and **immunohistochemistry** testing (see callout box **'Genetic testing in LBCL'**)

Genetic testing in LBCL

Genes and their associated mutations are commonly used to diagnose lymphoma. In addition, the presence or absence of certain mutations or other alterations in the genetic material of the tumour cells can help guide treatment and predict how likely a lymphoma is to respond to certain treatments. This science of identifying disease through DNA, genes, chromosomal translocations and mutations may be referred to as molecular profiling, genetic markers, genetic profiling, or driver gene-based classification.

2.4 Who will tell me about next steps, when, and how?

You will receive information from different members of your care team at different times throughout your treatment journey.

At the initial stages of treatment, a haematologist (or an oncologist, depending on your location) will explain the diagnosis, staging results, treatment plan, available therapies, and expected outcomes. They will also discuss any changes that may be needed if the lymphoma does not respond as expected to the therapy of your choice.

At this stage, you will likely also meet with a clinical nurse specialist or lymphoma nurse, who may be your main point of contact. Your nurse will be available to help you understand your test results and treatment instructions and answer questions between appointments, as well as being the one who take your blood, administers treatments, and helps you with other practical aspects of your care (including those related to any adverse events you may experience).

Information surrounding your care may be communicated in person, by phone, or through written treatment summaries provided after key appointments. If you are unsure about the next step(s) or have not heard about an upcoming appointment, you should contact your nurse or the hospital for clarification.

SECTION **2.**

2.5 How will treatment affect my quality of life – what is the risk of adverse events and how will these be managed?

2.5.1 Quality of life

Quality of life is key in the treatment of LBCL. However, all cancer treatments are different, and each approach to treatment can affect your life in different ways. How much a particular treatment will extend your life is not the only factor to consider when you are thinking about different treatment options. You will also need to look at how a treatment will affect your overall wellbeing – your quality of life.

2.5.2 Common concerns, common problems

In a survey conducted by Lymphoma Coalition, patients reported a number of the more common concerns surrounding treatment for LBCL, including fear of cancer progression/**relapse** of lymphoma, concerns surrounding being immunocompromised, anxiety/nervousness, depression/sadness, and concerns about body image/physical appearance.10 If you are experiencing any of these concerns, or others, it is important that you discuss them with your care team, as there are a number treatment- and lifestyle-focused options that have been shown to help support physical and emotional wellbeing during cancer care.

For many patients, being better informed about their lymphoma and treatment is a step towards alleviating potential concerns, misunderstandings, or a lack of information that can contribute to stress, anxiety, and depression surrounding cancer treatment.

2.5.3 Managing fatigue

Many patients (up to 66%) experience fatigue as an effect of treatment. Sometimes fatigue is also a symptom of the lymphoma itself.10 You should let your care team know if you are experiencing fatigue as they can request tests to ensure your tiredness and weakness is not caused by something else, like anaemia or an infection.

Fatigue may also be related to anxiety or sadness you feel due to your diagnosis and treatment. While treating any underlying condition can relieve your fatigue, certain habits can also help, such as exercise, and time-management that focuses activities to the times of the day when you feel your best.

"In a survey conducted by Lymphoma Coalition, 72% of patients surveyed found that, since their diagnosis of lymphoma or CLL, they had made positive changes to their lifestyle (e.g., dietary changes, less use of alcohol, fewer working hours, exercise) to support their treatment, with many patients (94%) reporting that they were able to maintain positive lifestyle changes in the longer-term."

2.6 Will my priorities, values, beliefs, and goals be taken into account during treatment?

Your care team can offer information on the various treatments available. Before you make any decisions surrounding treatment, it is important to consider personal priorities, values, beliefs, and goals. Think carefully about your personal treatment goals and how cancer treatment can affect quality of life for both you and those who care about you and be ready to discuss this with the care team.

"Successful treatment is about more than just treating the cancer; it's about balancing the level of care with the quality of life of both the patient and those who care about them."

SECTION **3.**

WHAT ARE MY TREATMENT OPTIONS?

Treatment of any cancer is based on professional guidelines that provide evidence-based recommendations for the diagnosis, treatment, follow-up, and supportive care of patients with LBCL in Europe.[2]

3.1 What treatment can I expect and why has this been recommended?

While the specific LBCL subtype is a consideration when assessing care options, treatment is also guided by a number of additional factors including tumour location, stage and size, findings from tests (e.g., imaging and molecular/genetic testing), and a number of other disease- and patient-specific factors such as the presence/absence of risk factors, patient age and 'fitness', genetic factors that can influence response to treatment, and response to previous therapies (if applicable).

3.2 Will treatment be in a specialist cancer centre or a regular hospital?

Most people with LBCL receive their treatment in a hospital-based haematology unit, usually as **outpatients**. This means you come to the hospital for your treatment and can go home the same day. However, you may need to stay in hospital for short periods at certain points in your treatment. Chemotherapy and immunotherapy are usually given during scheduled visits to the day unit. Your doctor may decide to admit you to hospital, especially during the first cycles, so they can monitor you more closely for adverse events and make sure you are safe and well. Note that, for certain intravenous therapies, your care provider may recommend implanting an infusion device (i.e., a port), which can reduce the number of needle-sticks a patient receives during treatment.

Some treatments requiring specialised centres include CAR-T cell therapy, stem cell (bone marrow) transplantation, certain **clinical trials**, and treatments to manage rare or high-risk types of LBCL (e.g., those with CNS involvement)

Your care team will let you know if you need treatment at a specialist centre and coordinate any referrals. Regardless of where treatment takes place, the goal is to ensure you have access to a full multidisciplinary team with experience managing your LBCL.

SECTION **3.**

3.3 One size fits… most patients?

Despite there being different types of LBCL, the majority of patients diagnosed with an LBCL are treated with the same first-line approach (this includes patients with transformation from previously untreated or unknown indolent lymphomas to an LBCL). This approach to treatment is based on extensive clinical study, is according to treatment guidelines, and is built around a combination of chemotherapy, immune-based therapy, and supportive steroid therapy named 'R-CHOP' (see **Table 2: First-line treatment options**).

There are, however, notable exceptions – for example, patients with a diagnosis of high-grade double-hit or triple-hit DLBCL, an aggressive subtype characterized by genetic rearrangements in the MYC gene combined with BCL2 and/or BCL6 genes, and patients with primary mediastinal B-cell lymphoma, primary testicular lymphoma, or intravascular LBCL, and those with LBCL at high risk for CNS relapse, may be recommended an alternative first-line of therapy. In the case of a diagnosis of any of these specific subtypes, you can speak with your care team about your treatment options (see **Figure 2: Treatment protocols according to LBCL (sub)type and patient profile**)

It is also possible that your care team will discuss the possibility of inclusion in a clinical trial at a first-line treatment option (See **Section 3.8 entitled Are clinical trials an option and what would that mean for me?**)

"Combination treatments are usually based on the initial of each drug included – for example, R-CHOP comprises the monoclonal antibody rituximab (R), the chemotherapy agents cyclophosphamide (C), hydroxydaunorubicin (H), vincristine (O, based on the more common brand name for the drug), and prednisone (P). Speak with your care team if you would like more information on the specific components of your treatment combination."

TABLE **2 -** FIRST-LINE TREATMENT OPTIONS

Table 2 shows the main options for the first-line treatment of LBCL (i.e., treatment options in patients with newly diagnosed LBCL that has not been treated previously). Note that this is not an exhaustive list of all first-line available treatment options; other treatment protocols exist and will be discussed by the care team if relevant to your individual diagnosis.

CLASS OF THERAPY	BRIEF EXPLANATION
Chemo-immunotherapy combination therapy	Chemotherapy combined with immunotherapy
Steroids (also 'prephase corticosteroid therapy')	
Inclusion in a clinical trial	Clinical trials are research studies that test new treatments or new combinations of treatments. They offer access to innovative therapies that may not yet be widely available

AGENTS	LINE OF THERAPY
(these are specific combinations of drugs, and the choice of which one is recommended to you depends on individual factors)	
• R-CHOP • Pola-R-CHP • DA-EPOCH-R • R-COEP • R-GCVP • R-COMP • R-GemOx	Chemotherapy and immunotherapy combination therapy is used in the first line in the majority of patients with LBCL, with the combination being determined by disease- and patient-specific risk factors R-CHOP is the most common first-line therapy in LBCL and represents a combination of three types of chemotherapy (cyclophosphamide, hydroxydaunorubicin, vincristine), a monoclonal antibody (rituximab), and a steroid (prednisone; see Steroids below)
• Prednisone/prednisolone • Dexamethasone • Methylprednisolone	Steroid treatment is recommended to support first-line treatment and to reduce the likelihood of specific treatment-related adverse events
A list of clinical trials specific to LBCL subtypes and that are active or currently recruiting is available at the EU Clinical Trials Register: https://clinicaltrials.eu/disease/diffuse-large-b-cell-lymphoma/	Participation in a clinical trial does not mean you are running out of options – trials may be offered at different stages of care While inclusion in a clinical trial is not standard of care, a clinical trial may be offered if standard treatment is not the best option in your situation

3.4 Treatment protocols according to LBCL (sub)type and patient profile

FIGURE **2** - TREATMENT PROTOCOLS ACCORDING TO LBCL (SUB)TYPE AND PATIENT PROFILE

Figure 2 shows the main options for the first-line treatment of LBCL (i.e., treatment options in patients with newly diagnosed LBCL that has not been treated previously). Treatment is based on several disease- and patient-specific factors including the type of lymphoma, the stage of the disease, and risk factors. If you are uncertain of your individual diagnosis, contact your care team and request additional information.

Profile 1: All patients with LBCL according to risk factors

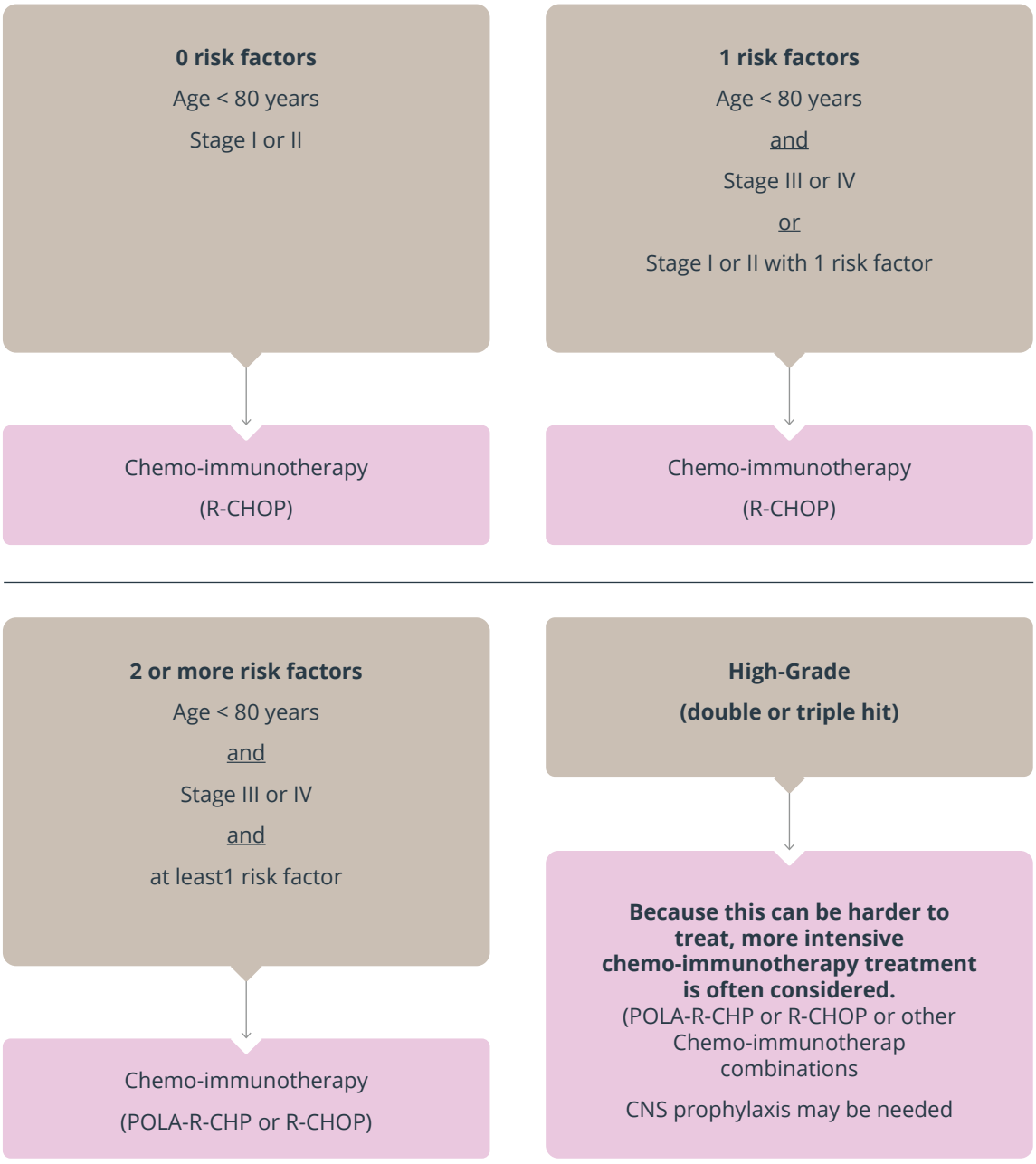
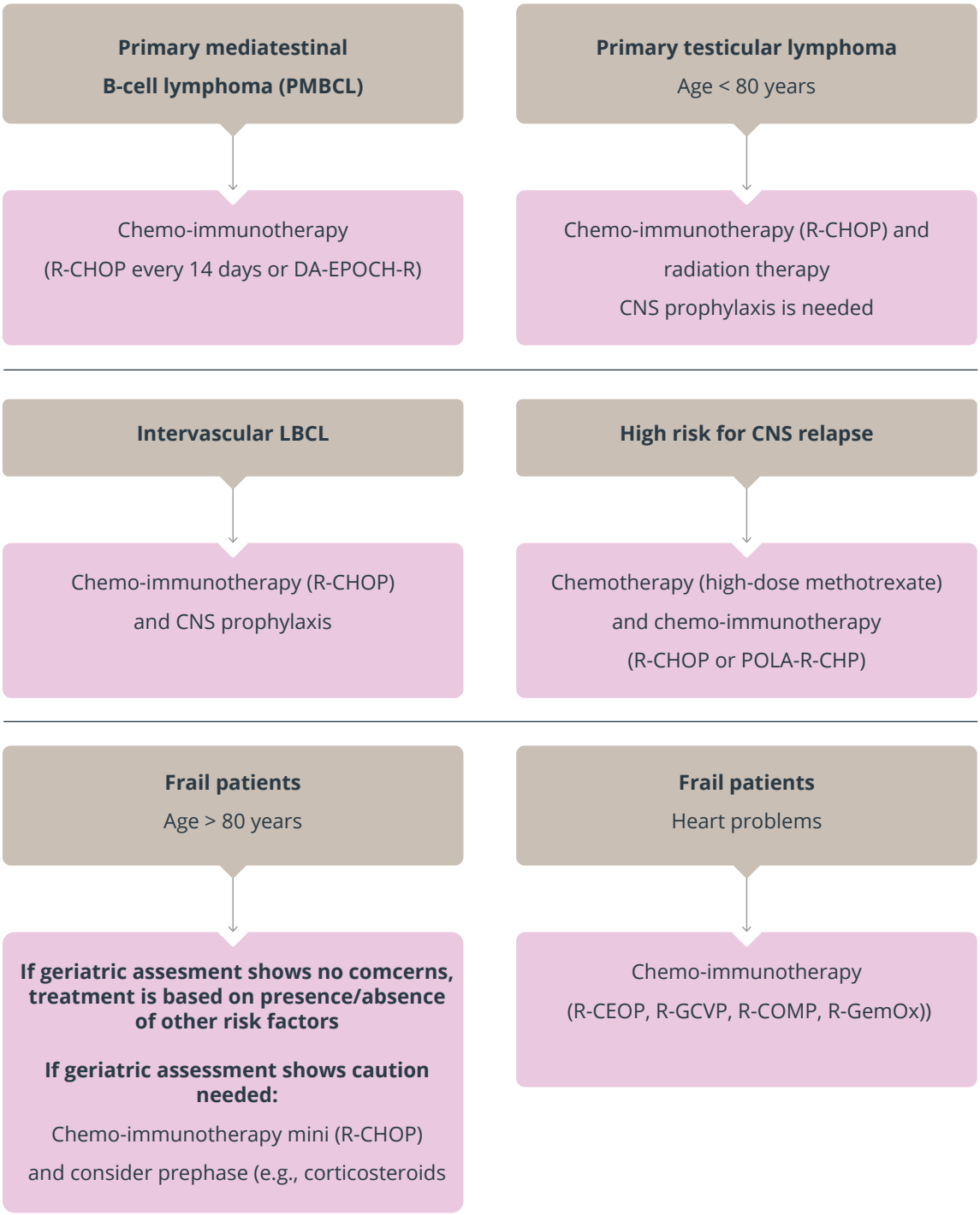


FIGURE **2 -** TREATMENT PROTOCOLS ACCORDING TO LBCL (SUB)TYPE AND PATIENT PROFILE

Note: A clinical trial may also be offered if standard treatment is not the best option in your situation, your lymphoma has returned or not responded to previous therapy, or your medical team believes you may benefit from a new therapy being studied. If you think you are eligible, or would benefit from involvement in a clinical trial, please talk with your care team.

Profile 2: By disease subtype (includes age/frailty and results of CNS assessment)



3.5 What is the likelihood of needing further treatment after this initial round of therapy – might the cancer come back?

Treatment in the period immediately following diagnosis may feel overwhelming, but individualized treatment with regular follow-up provides the greatest chance of treatment success. However, there is also a need for long-term follow-up to mitigate the likelihood of future disease- or treatment-related issues.

For approximately 30–40% of patients with LBCL, the lymphoma comes back after a period of remission (called a relapse), or the lymphoma does not respond to treatment as expected (called refractory disease) after first-line treatment.2

Treatment recommendations for relapsed/refractory LBCL are influenced by the length of time the lymphoma was in remission following the previous treatment and the individual profile of the patient (see **Table 3: Treatment options used alone or in combination in relapsed/refractory LBCL and Figure 3: Second-line treatment protocols according to LBCL treatment response**).

A biopsy will be performed ahead of additional lines of treatment to confirm that the physical findings/imaging results are still due to LBCL (i.e., to be sure the lymphoma hasn't changed), rather than other cancers, another type of lymphoma requiring a different treatment, or another illness. You may be recommended for biopsy more than once, depending on your response to treatment.

Your care provider will inform you on any 'red flags' suggesting signs of possible symptoms or relapse/progression, and urgent contact details in these occurrences.

TABLE **3 -** TREATMENT OPTIONS USED ALONE OR IN COMBINATION IN RELAPSED/REFRACTORY LBCL

Table 3 shows the main treatment options for relapsed/refractory LBCL (i.e., treatment options in patients with LBCL that has returned following previous rounds of therapy or that has not responded to initial therapy).

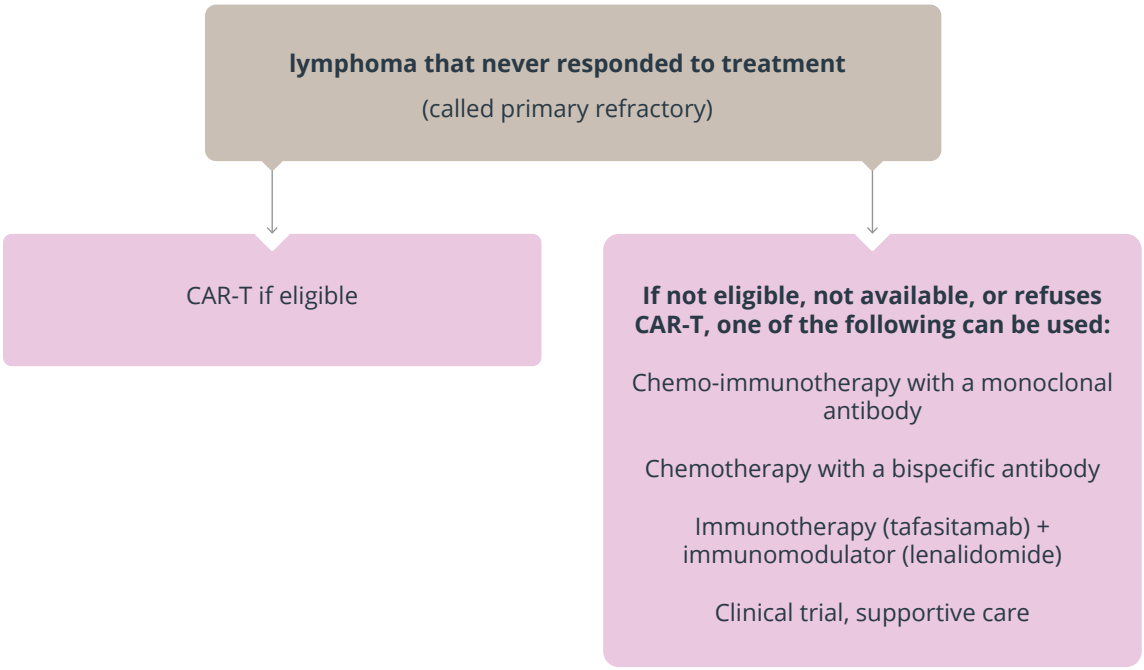
CLASS OF THERAPY	BRIEF EXPLANATION
CAR T-cell therapy	A type of treatment in which a patient's T cells (a type of immune system cell) are changed in the laboratory so they will attack cancer cells. Also called chimeric antigen receptor T-cell therapy
Monoclonal antibodies	Monoclonal antibodies help the immune system recognise specific targets
Bispecific antibodies	A type of antibody that can bind to two different antigens at the same time
Antibody–drug conjugates (ADCs)	A substance made up of a monoclonal antibody chemically linked to a drug Also called ADCs
Immunomodulating agents/ immunomodulation	A substance that stimulates or suppresses the immune system and may help the body fight cancer, infection, or other diseases. Also called immune system modulator
High-dose therapy followed by autologous stem cell transplant (ASCT)	An autologous stem cell transplant replaces a patient's stem cells that were destroyed by treatment with radiation or high doses of chemotherapy
Radiation therapy	The use of high-energy radiation from x-rays, gamma rays, neutrons, protons, and other sources to kill cancer cells and shrink tumours Also called irradiation and radiotherapy

AGENTS	LINE OF THERAPY
• Anti-CD19 chimeric-antigen receptor cells	CAR T-cell therapy is recommended when disease relapses within one year following first-line treatment or when the lymphoma does not respond to first-line treatment
• Tafasitamab	Antibody-based and immunomodulator-based treatment protocols are either used in combination with chemotherapy as a first-line treatment (i.e., rituximab in R-CHOP) or are recommended when disease relapses or does not respond to first-line treatment (e.g., tafasitamab and lenalidomide in primary refractory lymphoma loncastuximab tesirine in lymphoma returned after more than 1 year)
• Glofitamab • Epcoritamab • Odronextamab"	
• Polatuzumab vedotin • Loncastuximab tesirine"	
• Lenalidomide	
	ASCT is often recommended when disease relapses after more than one year to support treatment and to reduce the likelihood of specific treatment-related adverse events
	Radiation therapy may be recommended if there is limited amount of lymphoma, and as support to other treatments

FIGURE **3 -** TREATMENT FOR RELAPSED/REFRACTORY LBCL ACCORDING TO YOUR INDIVIDUAL RISK PROFILE (SECOND-LINE TREATMENT)

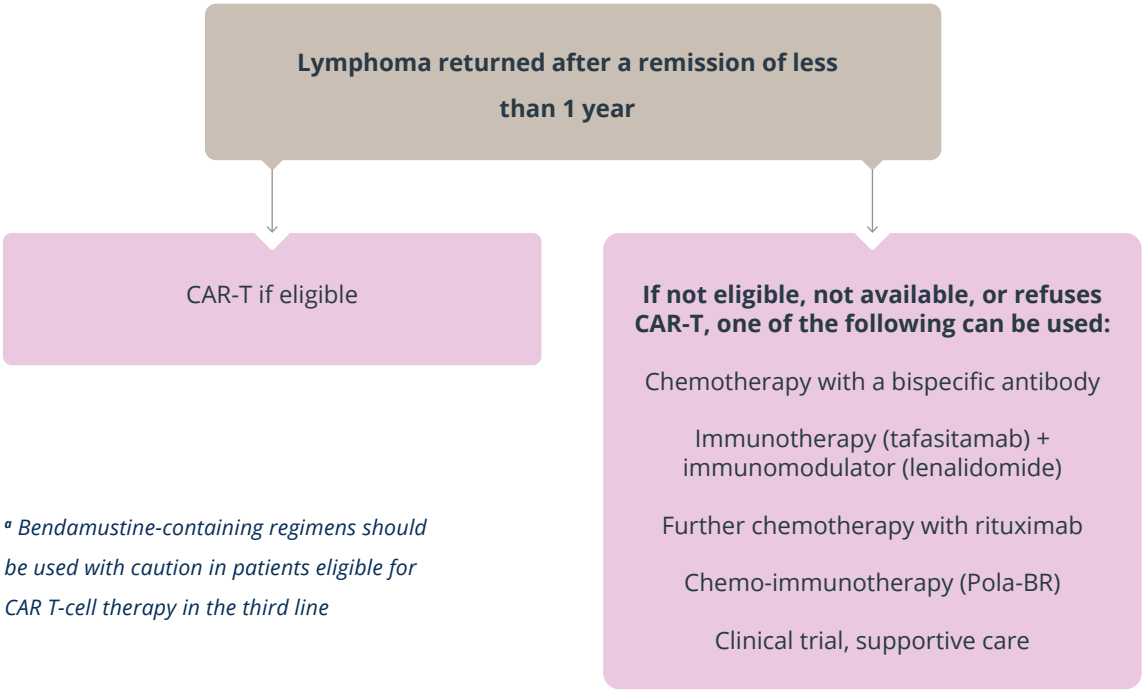
Figure 3 shows the main treatment options for relapsed/refractory LBCL (i.e., treatment options in patients with LBCL that has returned following previous rounds of therapy or that has not responded to initial therapy). Treatment is based on several disease- and patient-specific factors including the duration of remission and eligibility/willingness for specific therapies. If you are uncertain of your individual diagnosis, contact your care team and request additional information.

Profile 1: Lymphoma never responded to treatment



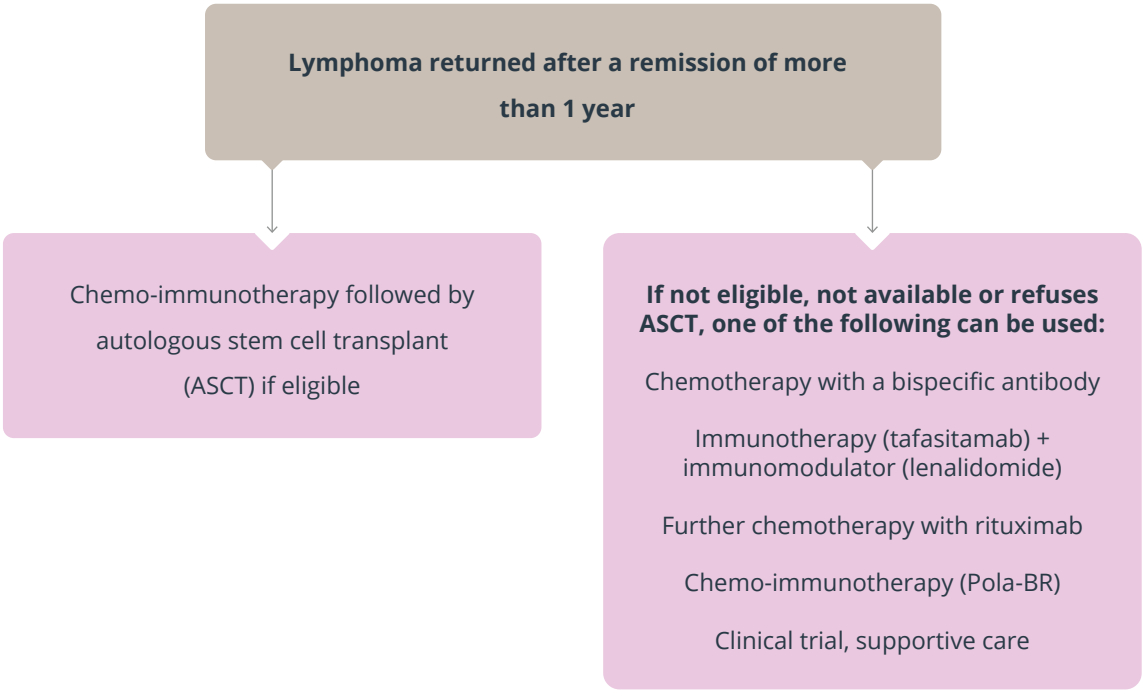
Note: A clinical trial may also be offered if standard treatment is not the best option in your situation, your lymphoma has returned or not responded to previous therapy, or your medical team believes you may benefit from a new therapy being studied. If you think you are eligible, or would benefit from involvement in a clinical trial, please talk with your care team.

Profile 2: Lymphoma returned after a remission of less than 1 year



[a] Bendamustine-containing regimens should be used with caution in patients eligible for CAR T-cell therapy in the third line

Profile 3: Lymphoma returned after a remission of more than 1 year



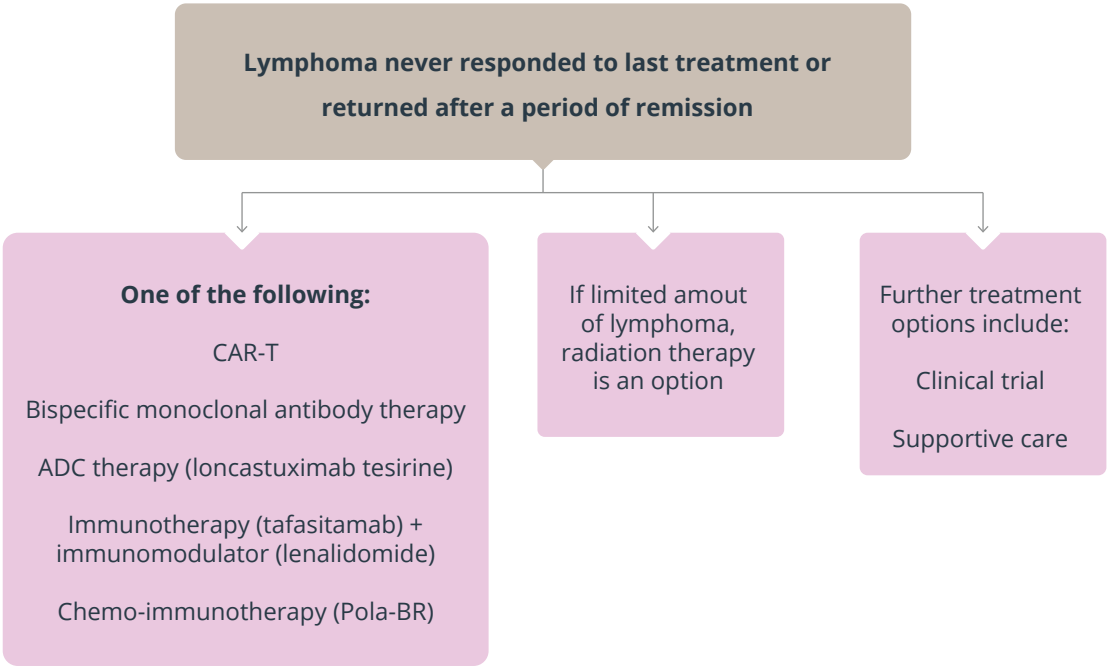
SECTION **3.**

3.7 Treatment in the event of continued relapse (third-line treatment onwards)

As with second-line treatment, recommendations for further lines of treatment are influenced by previous treatments, the lymphoma, and the patient's overall health. Again, the patient will likely be recommended for further biopsy to confirm that the physical findings/imaging results are still due to LBCL; see Figure 4. Treatment in the event of continued relapse (third-line treatment onwards).

Figure 4 shows the main treatment options for patients with LBCL with continued relapse (i.e., patients with LBCL that has returned following second-line treatment or that has not responded to second-line therapy). Treatment is based on several disease- and patient-specific factors including eligibility/willingness for specific therapies. If you are uncertain of your individual diagnosis, contact your care team and request additional information.

Figure 4: Treatment in the event of continued relapse (third-line treatment onwards)



Note: A clinical trial may also be offered if standard treatment is not the best option in your situation, your lymphoma has returned or not responded to previous therapy, or your medical team believes you may benefit from a new therapy being studied. If you think you are eligible, or would benefit from involvement in a clinical trial, please talk with your care team.

SECTION **3.**

3.8 Are clinical trials an option and what would that mean for me?

Clinical trials are research studies. Often, they test new treatments or new combinations of treatments. They offer access to innovative therapies that may not yet be widely available.

A clinical trial may be offered if standard treatment is not the best option in your situation, your lymphoma has returned or not responded to previous therapy, or your medical team believes you may benefit from a new therapy being studied. Before joining a trial, you will go through an informed consent process, where the research team will explain the purpose of the study, the treatment being tested, the possible risks and benefits of the trial, and how your health will be monitored. Taking part in a trial is voluntary, and you can withdraw at any time. Many patients find that participating helps them feel more involved in advancing lymphoma research.

If you think you are eligible, or would benefit from involvement in a clinical trial, please talk with your care team. Note that inclusion in any clinical trial is often limited to patients with a very specific combination of disease- and patient-factors, that there may be risks associated with trial-stage treatments, and that inclusion in trial does not equate to better treatment or a more advanced level of care. Your care team will advise you on your suitability for inclusion in a clinical trial, and, if you are enrolled, you will likely continue to receive standard of care in addition to any trial-specified protocols.

SECTION **4.**

WHAT HAPPENS AFTER MY TREATMENT IS FINISHED?

4.1 I know what to expect in the coming weeks and months – can we talk in terms of years?

Treatment planning is focused on long-term approaches to goal setting that provide clarity to your treatment journey. While it is important to focus on your immediate care today, it is also important that your care providers build a comprehensive roadmap for your health that extends beyond the coming weeks and into the next several years.

4.1.1 Long-term or late adverse events

Some patients experience long-term or late adverse events after completing treatment. These may include heart effects related to specific treatments, nerve changes such as tingling or numbness in the hands or feet (called peripheral neuropathy), difficulties with memory or cognitive changes such as trouble concentrating (usually referred to as 'chemo brain'), endocrine issues including thyroid or hormonal changes, and immune system suppression, which may increase infection risk in the months after treatment. Your care team will discuss which long-term effects are most relevant to your individual care plan, and how they can be monitored or treated.

Note that some treatments (including CAR T-cell therapy, stem cell transplantation, and some chemotherapies) have been associated an increased risk of secondary cancers. If you are eligible for treatment with any of these therapies, your care team will discuss the risks with you before treatment is initiated.

If you notice new or ongoing symptoms at any point — even many years after treatment — let your care team know. Reporting concerns is an important part of your long-term care, and there are ways to assess, manage, or treat many late effects.

In addition, fatigue can be persistent in the treatment of DLBCL, and screening is usually warranted to ensure that there is no underlying cause. You will also be given information on cancer-related fatigue and coping mechanisms should you experience this as a longer-term adverse event (see Section 4.2 entitled **What about my emotional health, will I receive ongoing support?**)

4.1.2 Duration of follow-up

Patients with LBCL and who are event-free at 2 years after the initial diagnosis have comparable overall survival to that of the general population, meaning the first two years from diagnosis are considered key to successful follow-up.3

The initial 2-year period of follow-up will include ongoing clinical examination and management of any long-term adverse events related to treatment. You will also be referred for regular blood count assessment during this initial 2-year period, and cardiology tests may be recommended within the first year of treatment, then at 3 and 5 years, and then every 5 years, depending on the type of treatment you received.

In addition, physical examination for at least 2 years is recommended in patients treated with anthracyclines and/or radiotherapy, with particular attention being paid to assessments monitoring for the development of secondary tumours or other long-term adverse events associated with these treatments.

You will likely be offered an end-of-treatment consultation, which should include a holistic needs assessment and associated written care plan with a comprehensive treatment summary. At this time, both the patient and their general practitioner should be made aware of follow-up plans and potential future disease or treatment-related issues.

After 5 years of relapse-free follow-up, patients are considered to be cured. Late relapses can occur but are very rare.[3]

4.2 What about my emotional health, will I receive ongoing support?

Patients often present with complex needs, and involvement of key members of the wider care team (e.g., lymphoma clinical nurse specialists, pharmacists, cardiorespiratory specialists focused on your heart health and your breathing, and healthcare of older people liaison teams) can prove to be very helpful.

Everyone, no matter your age or general health/wellbeing at diagnosis, will be offered support to address any concerns you may have surrounding your treatment. You will likely be offered an emotional distress assessment which, at a minimum, will be performed at every treatment milestone (including at diagnosis, when treatment starts, and when treatment ends) or in the case or relapsed/refractory disease. Identifying distress early allows for timely referral to psychological and supportive care services. You may also be referred for additional screening for other cancer types.

Psychological concerns such as anxiety and fear of recurrence are frequent. Being diagnosed with any cancer can be overwhelming – physically, emotionally, personally, and professionally. It is normal to experience emotional challenges such as anxiety, fear of recurrence, or low mood after treatment. Many patients describe the post-treatment period as unexpectedly difficult. Your care team may offer psychological screening using validated tools such as the NCCN Distress Thermometer,11 referral to psycho-oncology services, counselling or patient support groups, access to a clinical nurse specialist for ongoing emotional support, and peer support through lymphoma organisations such as Lymphoma Coalition. If you are struggling emotionally, tell your care team, they can connect you with appropriate support services.

In addition, Lymphoma Coalition has produced a series of publications, videos, and practical tools to support patients undergoing treatment for lymphoma that will help you to understand the psychological impact of lymphoma, and take you beyond the diagnosis to discuss subjects such as talking with your care team about your emotional needs and how honest dialogue improves lymphoma care, self-care strategies, and why care doesn't end when treatment does. These can be found online at lymphomacoalition.org.

SECTION **5.**

GLOSSARY AND RESOURCES[12]

- **Antibody–drug conjugate:** A substance made up of a monoclonal antibody chemically linked to a drug. The monoclonal antibody binds to specific proteins or receptors found on certain types of cells, including cancer cells. The linked drug enters these cells and kills them without harming other cells. Some antibody-drug conjugates are used to treat cancer. Also called ADCs.

- **Autologous stem cell transplant (ASCT):** A procedure in which a patient's healthy stem cells (blood-forming cells) are collected from the blood or bone marrow before treatment, stored, and then given back to the patient after treatment. An autologous stem cell transplant replaces a patient's stem cells that were destroyed by treatment with radiation or high doses of chemotherapy. An autologous stem cell transplant is most often used to treat blood cancers, such as leukaemia and lymphoma.

- **Bispecific antibody:** A type of antibody that can bind to two different antigens at the same time. Bispecific antibodies are being studied in the imaging and treatment of cancer. They are made in the laboratory.

- **B lymphocytes:** A type of white blood cell that makes antibodies. B lymphocytes are part of the immune system and develop from stem cells in the bone marrow. Also called B cells.

- **T lymphocytes:** A type of white blood cell. T lymphocytes are part of the immune system and develop from stem cells in the bone marrow. They help protect the body from infection and may help fight cancer. Also called T cell and thymocyte.

- **CAR T-cell therapy:** A type of treatment in which a patient's T cells (a type of immune system cell) are changed in the laboratory so they will attack cancer cells. T cells are taken from a patient's blood. Then the gene for a special receptor that binds to a certain protein on the patient's cancer cells is added to the T cells in the laboratory. The special receptor is called a chimeric antigen receptor (CAR). Large numbers of the CAR T cells are grown in the laboratory and given to the patient by infusion. CAR T-cell therapy is used to treat certain blood cancers, and it is being studied in the treatment of other types of cancer. Also called chimeric antigen receptor T-cell therapy.

- **Chemotherapy:** Treatment that uses drugs to stop the growth of cancer cells, either by killing the cells or by stopping them from dividing. Chemotherapy may be given by mouth, injection, or infusion, or on the skin, depending on the type and stage of the cancer being treated. It may be given alone or with other treatments, such as surgery, radiation therapy, or biologic therapy.

- **Chemo-immunotherapy:** Chemotherapy combined with immunotherapy. Chemotherapy uses different drugs to kill or slow the growth of cancer cells; immunotherapy uses treatments to stimulate or restore the ability of the immune system to fight cancer.

- **CHOP regimen:** An abbreviation for a chemotherapy combination that is used to treat non-Hodgkin lymphoma and is being studied in the treatment of other types of cancer. It includes the drugs cyclophosphamide, doxorubicin hydrochloride (hydroxydaunorubicin), vincristine sulfate (Oncovin®), and prednisone.

- **Clinical trial:** A type of research study that tests how well new medical approaches work in people. These studies test new methods of screening, prevention, diagnosis, or treatment of a disease. Also called clinical study.

- **Clinically indolent lymphoma:** A type of lymphoma that tends to grow and spread slowly and has few associated symptoms.

- **Comorbidity:** The condition of having two or more diseases at the same time.
  Computed tomography (CT): CT is a non-invasive imaging procedure that uses special x-ray equipment to create detailed pictures, or scans, of areas inside the body.

- **Chromosomal translocation:** Chromosomal translocation in LBCL can be thought of as a genetic 'mix-up' where pieces of chromosomes break off and swap places, causing the cell to behave abnormally and grow uncontrollably.

- **Genetic testing:** A laboratory method that looks for changes in genes, gene expression, or chromosomes in a person's cells or tissues.

- **Histological transformation:** A change from one cell type to another, histologic transformation (HT) refers to the evolution of a clinically indolent to a clinically aggressive lymphoma.

- **Immunohistochemistry:** A laboratory method that uses antibodies to check for certain antigens (markers) in a sample of tissue. The antibodies are usually linked to an enzyme or a fluorescent dye. After the antibodies bind to the antigen in the tissue sample, the enzyme or dye is activated, and the antigen can then be seen under a microscope. Immunohistochemistry is used to help diagnose diseases, such as cancer. It may also be used to help tell the difference between different types of cancer.

- **Immunomodulation:** Change in the body's immune system, caused by agents that activate or suppress its function.

- **Immunomodulating agent:** A substance that stimulates or suppresses the immune system and may help the body fight cancer, infection, or other diseases. Specific immunomodulating agents, such as monoclonal antibodies, cytokines, and vaccines, affect specific parts of the immune system. Nonspecific immunomodulating agents, such as BCG and levamisole, affect the immune system in a general way. Also called immune system modulator.

- **Line of therapy:** Your first course of treatment is called 'first-line treatment', with subsequent lines known as second-line therapy, third-line therapy, etc.

- **Lymphocyte:** A type of immune cell that is made in the bone marrow and is found in the blood and in lymph tissue.

- **Molecular subtype:** In cancer, a term used to describe the smaller groups that a type of cancer can be divided into, based on whether certain genetic changes or other biomarkers are present.

- **Molecular testing:** A laboratory method that uses a sample of tissue, blood, or other body fluid to check for certain genes, proteins, or other molecules that may be a sign of a disease or condition, such as cancer.

- **Monoclonal antibodies:** Monoclonal antibodies are immune system proteins that are created in the lab. Antibodies are produced naturally by your body and help the immune system recognise germs that cause disease, such as bacteria and viruses, and mark them for destruction. Like your body's own antibodies, monoclonal antibodies recognise specific targets.

- **Mutation:** A change (or 'error') in the DNA of B cells. In LBCL, certain mutations can affect genes that control how B cells grow, divide, and die. When these control mechanisms are disrupted, the cells can grow uncontrollably and form cancer. These mutations usually occur in the lymphoma cells only and are not typically inherited from a person's parents.

- **Magnetic resonance imaging (MRI):** A procedure that uses radio waves, a powerful magnet, and a computer to make a series of detailed pictures of areas inside the body.

- **Outpatient:** A patient who visits a health care facility for diagnosis or treatment without spending the night. Sometimes called a day patient.

- **Overall survival (rate):** The length of time from either the date of diagnosis or the start of treatment for a disease, such as cancer, that patients diagnosed with the disease are still alive. In a clinical trial, measuring the overall survival is one way to see how well a new treatment works. The overall survival rate is the percentage of people in a study or treatment group who are still alive for a certain period of time after they were diagnosed with or started treatment for a disease, such as cancer. The overall survival rate is often stated as a five-year survival rate, which is the percentage of people in a study or treatment group who are alive five years after their diagnosis or the start of treatment. Also called OS or survival rate.

- **Performance status:** A patient's level of functioning in terms of their ability to care for themselves, perform daily activities; often given as a score that is determined using a measure such as measured using the Eastern Cooperative Oncology Group Performance Status (ECOG PS) scale of the Karnofsky Performance Status (KPS) scale.

- **Positron emission tomography (PET):** PET uses small amounts of radioactive materials called radiotracers or radiopharmaceuticals, a special camera and a computer to evaluate organ and tissue functions. By identifying changes at the cellular level, PET may detect the early onset of disease before other imaging tests can.

- **Prognosis:** The likely outcome or course of a disease; the chance of recovery or recurrence.

- **Quality of life:** The overall enjoyment of life. Many clinical trials assess the effects of cancer and its treatment on the quality of life. These studies measure aspects of an individual's sense of well-being and ability to carry out activities of daily living.
  Radiation therapy: The use of high-energy radiation from x-rays, gamma rays, neutrons, protons, and other sources to kill cancer cells and shrink tumours. Radiation may come from a
- machine outside the body (external-beam radiation therapy), or it may come from radioactive material placed in the body near cancer cells (internal radiation therapy or brachytherapy). Systemic radiation therapy uses a radioactive substance, such as a radiolabelled monoclonal antibody, that travels in the blood to tissues throughout the body. Also called irradiation and radiotherapy.

- **Relapsed disease:** Return of a disease or the signs and symptoms of a disease after a period of improvement.

- **Refractory disease:** Disease that is stable (i.e., cancer that is neither decreasing nor increasing in extent or severity) or progressive (i.e., cancer that is growing, spreading, or getting worse).
  Staging: Performing exams and tests to learn the extent of the cancer within the body, especially whether the disease has spread from where it first formed to other parts of the body.

- **Steroid/corticosteroid:** Any of a group of lipids (fats) that have a certain chemical structure. Steroids occur naturally in plants and animals, or they may be made in the laboratory. Examples of steroids include sex hormones, cholesterol, bile acids, and some drugs.

SECTION **6.**

TRUSTED SUPPORT ORGANISATIONS, INCLUDING LOCAL/REGIONAL OPTIONS

6.1 Lymphoma Coalition member organisations

With ~100 member organisations from more than 55 countries, Lymphoma Coalition strives to be a central hub for resources and information sharing, providing important information for physicians, healthcare professionals, patients, and patient advocacy groups.

For more information on Lymphoma Coalition member organisations, visit our website at https://lymphomacoalition.org/member-organisation/, where you can find more information on international and local/regional organisations supporting patients with lymphoma, and access patient-friendly guidance that will help you better understand your lymphoma.

SECTION **6.**

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