

Diffuse large B-cell lymphoma

This information is about diffuse large B-cell lymphoma (DLBCL), the most common type of high-grade (fast-growing) non-Hodgkin lymphoma.

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We have separate information about the topics in **bold font**. Please get in touch if you'd like to request copies or if you would like further information about any aspect of lymphoma. Phone 0808 808 5555 or email information@lymphoma-action.org.uk.

What is diffuse large B-cell lymphoma (DLBCL)?

Lymphoma is a type of blood cancer that develops when white blood cells called **lymphocytes** grow abnormally. Lymphocytes are part of your **immune system**. They travel around your body in your **lymphatic system**, and help you fight infections and cancers. There are two types of lymphocyte: **T lymphocytes (T cells)** and **B lymphocytes (B cells)**. DLBCL involves the abnormal growth of B cells.

There are lots of different **types of lymphoma**. DLBCL is the most common type of **non-Hodgkin lymphoma**. It is a **fast-growing (high-grade) lymphoma**.

It is called diffuse large B-cell lymphoma because:

- it develops from abnormal B cells
- the abnormal cells are larger than normal, healthy B cells
- the abnormal cells are spread out (diffuse) rather than grouped together when they're examined under a microscope.

Who gets DLBCL?

Just under 5,500 people are diagnosed with DLBCL each year in the UK. It can develop at any age, but it's rare in children and is more common in older people. Most people diagnosed with DLBCL are 65 or over. DLBCL affects slightly more men than women.

In most cases, the **causes** of DLBCL are not known. Rarely, there is an association between DLBCL and **conditions affecting the immune system**. These include:

- **autoimmune conditions** like rheumatoid arthritis and systemic lupus erythematosus (DLBCL can develop as a result of long-term inflammation)
- **HIV**
- **organ transplantation**.

Sometimes DLBCL develops in people who have had a low-grade (slow-growing) lymphoma in the past. This happens when a low-grade lymphoma transforms (changes) into a quicker growing DLBCL. If this is the case for you, you might also find our information on **transformation** helpful.

Symptoms of DLBCL

Most people with DLBCL first notice painless lumps, often in their neck, armpit, groin or abdomen, or in your testicles if you're a man. These are **swollen (enlarged) lymph nodes**. They usually grow quite quickly, over just a few weeks. Sometimes, DLBCL can develop in lymph nodes deep inside your body where they can't be felt from the outside. The swollen nodes can form large lumps – known as 'bulky disease'. DLBCL can also develop outside

lymph nodes, called 'extranodal' disease. This affects around 4 in 10 people with DLBCL.

Thinking back, I noticed a huge lump on the left hand side of my groin. I went to see my doctor and was given antibiotics which didn't have any impact, so my doctor organised for me to go to hospital.

Leo, diagnosed with diffuse large B-cell lymphoma

The exact symptoms you experience depend on where in your body the DLBCL is. These are called **local symptoms**. They can be very variable depending on what organs or tissues are affected. For example:

- DLBCL in your stomach or bowel can cause tummy (abdominal) discomfort or pain, nausea, diarrhoea or bleeding. Around 1 in 4 people with DLBCL have lymphoma affecting the bowel.
- DLBCL in your chest can cause a cough or breathlessness. Fewer than 1 in 10 people with DLBCL have lymphoma involving the lungs.

Around 1 in 3 people with DLBCL experience fevers, night sweats and unexplained weight loss. These are known as 'B symptoms'. **Fatigue** and loss of appetite are also quite common.

Diagnosis and staging of DLBCL

The main way doctors diagnose DLBCL is to remove a swollen lymph node, or take a sample of tissue from it, and look at it under a microscope. This involves a small procedure called a **biopsy**, which is usually done under a local anaesthetic or by a small operation. The term biopsy is often used to refer to taking the sample and the tissue sample itself. The way a biopsy is carried out will depend on where the tissue sample is being taken from. The most common type of biopsy is called a core biopsy, which is where the needle is guided by ultrasound or CT scan. Sometimes a surgical excision biopsy is used to remove a larger section of tissue. The tissue sample is tested for particular proteins that are found on the surface of lymphoma cells. This can help your medical team to confirm the diagnosis and decide on the most appropriate **treatment** for you.

You will have **blood tests** to look at your general health, check your **blood cell counts**, make sure your kidneys and liver are working well and to rule out infections that could worsen when you have treatment. You will also have

blood tests to rule out infections that could be linked to your lymphoma, such as **HIV**, hepatitis B and hepatitis C.

You will have other tests and scans to find out which areas of your body are affected by lymphoma. This is called **staging**. Staging usually involves having a **PET scan**. If this isn't possible, you might have a **CT scan** instead.

Sometimes an **MRI scan** is done to look for lymphoma affecting the head or spine. If you have a CT scan, you might also have a sample of your bone marrow cells taken (a **bone marrow biopsy**), to check if you have lymphoma cells in your bone marrow. You might have a **lumbar puncture** to check if you have lymphoma cells in the fluid around your brain and spinal cord (cerebrospinal fluid, or CSF).

You usually have your tests done as an outpatient, so you shouldn't need to stay in hospital. You might need to stay in hospital if you are unwell. It takes a few weeks to get all the results back. **Waiting for test results** can be a worrying time, but it is important for your doctor to gather all of this information in order to plan the best treatment for you.

Types of DLBCL

There is some complex information in this section. However, not all of it will apply to you. You may wish to read only information that is relevant to you, or you might prefer to skip this section completely. If you are not sure what type of lymphoma you have, ask your medical team.

Most people with DLBCL do not have a specific type. This is called 'DLBCL not otherwise specified' or 'DLBCL NOS'. Even if you have DLBCL NOS, your biopsy sample might still be analysed to find the exact sort of B cell your lymphoma developed from. The main cell types are:

- germinal centre B cells (GCB)
- activated B cells (ABC).

At the moment, most people with DLBCL NOS have the same **treatment**. Scientists carrying out research have not shown that different treatments are effective against types of DLBCL that developed from different cells.

Rare types of DLBCL and other large B-cell lymphomas

Some people have a rare subtype of DLBCL or other large B-cell lymphoma. These subtypes are also detected by looking at your biopsy sample under a microscope and using specialist laboratory tests. They can cause some

different symptoms from the most common type of DLBCL but they may be treated in a similar way.

Rare types of DLBCL and other large B-cell lymphomas include:

- **primary mediastinal large B-cell lymphoma**
- **T-cell/histiocyte-rich large B-cell lymphoma**
- **EBV-positive DLBCL not otherwise specified**
- **intravascular large B-cell lymphoma.**

If you have been diagnosed with a rare type of DLBCL, you might want to read the sections below with for information about the different subtypes and the symptoms they cause. We also have separate information pages on:

- **rare types of high-grade B-cell lymphoma that are difficult to classify**, including DLBCL that has two or three genetic mutations (**double-hit or triple-hit lymphoma**)
- DLBCL that starts in your central nervous system (primary **CNS lymphoma**)
- DLBCL that only affects your skin (a type of **B-cell skin lymphoma**)
- DLBCL that develops in people who have **HIV**.

If you have been diagnosed with DLBCL that is not one of the specific rare subtypes, you might want to skip these sections.

Primary mediastinal large B-cell lymphoma (PMBL)

Primary mediastinal large B-cell lymphoma (PMBL) used to be classed as a subtype of DLBCL but it is now classed as a separate type of lymphoma. It typically affects people in their 20s and 30s. It is more common in women than men.

PMBL develops from B cells in the **thymus** (a small gland in your chest, behind your breastbone). It tends to grow as a large lump inside the chest where you can't see it or feel it. It can spread to lymph nodes but it doesn't usually spread to other parts of the body.

PMBL can cause symptoms by pressing on the lungs, gullet (oesophagus) or the large vein that carries blood from the body to the heart (the superior vena cava or SVC). It can also cause fluid to build up around the heart (pericardial effusion) or the lungs (pleural effusion). Symptoms might include:

- breathlessness

- cough
- difficulty swallowing
- swelling of the neck and face
- headaches
- dizziness.

Treatment for PMBL is similar to treatment for DLBCL with the usual addition of radiotherapy to the chest area. However, your medical team might suggest stronger treatment (such as **DA-EPOCH** plus **rituximab**) even if your lymphoma is at early-stage. You might be asked if you'd like to take part in a **clinical trial**.

T-cell/histiocyte-rich large B-cell lymphoma

T-cell/histiocyte-rich large B-cell lymphoma gets its name from the cells pathologists can see when they look at a biopsy sample under a microscope. It can develop at any age but it most commonly affects middle-aged men.

The most common symptoms are:

- swollen lymph nodes
- swelling of the liver or spleen, which can cause tummy (abdominal) swelling and discomfort
- feeling generally unwell, with B symptoms (fever, night sweats and unexplained weight loss).

Under a microscope, T-cell/histiocyte-rich large B-cell lymphoma can look like **Hodgkin lymphoma**. It is important that it's diagnosed accurately, so you can have the most effective **treatment**.

Treatment for T-cell/histiocyte-rich large B-cell lymphoma is the same as for the most common type of DLBCL.

EBV-positive DLBCL not otherwise specified

This subtype of DLBCL typically develops in people over 50, although it can affect younger people. It is linked to a virus called Epstein–Barr virus (EBV), which infects B cells. Most people have been infected with EBV at some point in their lives, but it doesn't usually cause any symptoms. Only a very small number of people who have had EBV go on to develop lymphoma. Scientists don't know why this is.

Symptoms of EBV-positive DLBCL depend on where the lymphoma is growing:

- Most people with EBV-positive DLBCL NOS (7 in 10) have lymphoma growing outside their lymph nodes (extranodal lymphoma), most commonly in the skin, lungs, tonsils or stomach. The **symptoms** you have depend on where in your body the lymphoma is growing.
- Some people (3 in 10) have lymphoma only in their lymph nodes.

Treatment for EBV-positive DLBCL is the same as for DLBCL NOS.

Intravascular large B-cell lymphoma

This lymphoma mainly affects older adults. The abnormal lymphocytes are found within small blood vessels called 'capillaries'.

This subtype of lymphoma doesn't usually cause enlarged lymph nodes. The exact symptoms depend on which capillaries are affected, but might include:

- nervous system symptoms such as confusion, seizures, dizziness or weakness
- reddened patches or lumps in the skin
- B symptoms (fever, night sweats, unexplained weight loss)
- enlarged liver or spleen.

Treatment for intravascular large B-cell lymphoma is the same as for DLBCL NOS.

Outlook for DLBCL

At any stage, DLBCL is usually treated with the aim of curing it. It often responds well to treatment and many people go into **complete remission** (no evidence of lymphoma).

Your specific outlook depends on the **stage** of your lymphoma, the exact type of DLBCL you have, your general health and many other individual factors. Your lymphoma specialist is the best person to talk to about the likely outcome of your treatment. They can use the results of your tests and other individual factors (for example, your age and how fit you are) to calculate a score that helps predict how likely you are to respond to a particular treatment.

Survival statistics can be confusing as they don't tell you what your **individual** outlook is – they only tell you how a group of people with the same diagnosis did over a period of time. Remember that treatments are improving all the time and survival statistics are usually measured over 5 or 10 years after treatment. This means that statistics only tell you how people did in the past. Those

people may not have received the same treatment as you. Because of this variability, many people do not find survival statistics helpful.

If you want to know more about survival statistics for DLBCL, [Cancer Research UK](#) have some information that you might find useful.

Treatment of DLBCL

If you are under 18, or are a parent or carer of someone under 18 who has DLBCL, our section on [lymphoma in children](#) has more information on treatment in this age group. Young people (up to 24) with DLBCL might find our section on [lymphoma in young people](#) more helpful.

The treatment your medical team recommends for you depends on the stage of your lymphoma and the signs and symptoms you have. [Stage 1](#) or [stage 2](#) DLBCL is known as 'early-stage' lymphoma. [Stage 3](#) or [stage 4](#) DLBCL is known as 'advanced-stage' lymphoma. Most people have advanced-stage DLBCL when they are diagnosed. Treatment is different depending on whether you have [early-stage lymphoma](#) or [advanced-stage lymphoma](#).

When choosing your treatment, your team also takes into account:

- your age
- other illnesses you might have
- your general health and fitness
- your feelings about treatment
- factors that may be important to you in the future
- the available treatment options, including clinical trials.

Your doctor also considers any potential [side effects](#), including long-term or [late effects](#) (health problems that develop months or years after treatment) of the treatment. Your medical team should explain the possible side effects and late effects of your planned treatment.

Treatment of early-stage DLBCL

Three in ten people with DLBCL have early-stage DLBCL (stage 1 or stage 2) and are treated with a short course of [chemotherapy](#) given with [antibody therapy](#) (chemo-immunotherapy), followed by [radiotherapy](#) to the areas affected by lymphoma.

The most commonly used **chemotherapy regimen** (combination of drugs) is **R-CHOP**: rituximab, cyclophosphamide, hydroxydaunorubicin (doxorubicin), vincristine (also known as **Oncovin®**) and prednisolone.

You have all of the drugs through a drip into a vein (intravenously) on the first day of treatment, apart from prednisolone, which is given as tablets over 5 days. Most people have the intravenous treatment as an outpatient and go home the same day.

The drugs are given in cycles lasting 21 days, including the 5 days of treatment followed by a rest period for your body to recover before the next cycle. The exact number and duration of these cycles will depend on your lymphoma and what other treatments you have. Most people who have R-CHOP will also have a treatment called a **growth factor**, which involves daily injections under the skin for a few days to lower the risk of infection. These injections are given at home by a district nurse or a carer/relative. You can also give them to yourself.

- Many people with early-stage DLBCL have three to four cycles of 'short-course' R-CHOP followed by **radiotherapy**.
- If radiotherapy is not possible (usually because the areas involved with lymphoma are too far apart), treatment with six cycles of 'full course' R-CHOP is recommended.
- Some people with early-stage DLBCL can avoid radiotherapy if they are 'low-risk' based on their age, fitness, blood test results and non-bulky disease, or if they have a complete response to R-CHOP. Such patients do very well with four cycles of R-CHOP.

After your course of R-CHOP for early-stage DLBCL, you might have radiotherapy to the area affected by lymphoma, particularly if you have areas of bulky disease. This is based on your individual circumstances. Your specialist should talk to you about the possible risks and benefits of radiotherapy in your individual situation.

Treatment of advanced-stage DLBCL

Advanced-stage DLBCL (stage 3 and 4) is usually treated with six cycles of **Pola-R-CHP**:

- **polatuzumab vedotin** – a type of treatment called an antibody–drug conjugate: an antibody joined to a strong anti-cancer drug. The antibody sticks to protein called CD79b on the surface of B cells. This carries the drug directly to the B cells and kills them.

- rituximab,
- cyclophosphamide, hydroxydaunorubicin (doxorubicin), vincristine (also known as **Oncovin®**) and prednisolone.

Other options for treatment include six cycles of R-CHOP, or, if you are not well enough to have full strength chemo-immunotherapy, you might have an adjusted regimen such as:

- Dose reduced Pola-R-CHP or R-CHOP – in which the dose of some drugs might be reduced.
- RGCVP – in which one of the drugs (doxorubicin) is replaced with gemcitabine as this is a safer option in people with severe heart disease or risk factors for heart disease.
- Treatment on a clinical trial.

If you are at high risk of your lymphoma coming back (**relapsing**), or if you have a particularly aggressive subtype, your doctor might recommend a more intensive treatment depending on your age and fitness to tolerate stronger treatment. It's important to note that these treatments have more side effects and doctors don't yet know for sure that they are more effective. These stronger treatments include:

- **R-CODOX-M/R-IVAC:** rituximab plus cyclophosphamide, vincristine (**Oncovin®**), **doxorubicin** and **methotrexate** / rituximab plus ifosfamide, etoposide (**VP-16**) and cytarabine (**Ara-C**).
- **DA-EPOCH-R:** dose-adjusted etoposide, prednisolone, vincristine (**Oncovin®**), cyclophosphamide and doxorubicin (or hydroxydaunorubicin) plus rituximab.

Most people with advanced-stage DLBCL do not have **radiotherapy**. However, you might have radiotherapy if:

- you have lymphoma left in just one area of your body after your chemotherapy
- you have bulky disease – the radiotherapy can help prevent the lymphoma relapsing (coming back) in these areas.

CNS prophylaxis in DLBCL

Around 1 in 20 people have DLBCL that comes back (relapses) in their central nervous system (CNS – your brain and spinal cord) after going into remission. If this happens, the lymphoma can be very difficult to treat.

If your doctor thinks you have a high risk of DLBCL affecting your CNS, you might be given treatment to try and prevent this. This is called 'CNS prophylaxis'. **Most people do not need CNS prophylaxis.** If you have been told you might benefit from it, you may want to look at our separate [information on CNS prophylaxis](#).

Follow-up of DLBCL

You will have a [scan](#) when you finish your treatment to see how you have responded. This is usually a PET/CT scan. You might also have other tests. Your doctor can use the results of the scan and other tests, if needed, to see if you are in [remission](#) (no evidence of lymphoma) or if you need further treatment.

When you are in remission after treatment, you have regular [follow-up appointments](#). These are to check that:

- you are recovering well from treatment
- you have no signs of the lymphoma coming back (relapsing)
- you are not developing any [late effects](#) (side effects that develop months or years after treatment).

At each appointment, your doctor examines you and asks if you have any concerns or symptoms. You might have blood tests. You are unlikely to have a scan unless you have troubling symptoms.

You are usually seen every 3 months at first. If you are well, your appointments gradually become less frequent.

Most people are followed-up for 2 to 3 years after treatment for DLBCL. Some hospitals offer follow-up for 5 years or longer. You might have regular follow-up appointments, or you might be given guidance on [booking your own appointments](#) as-and-when you need them.

After your follow-up period ends, your GP usually becomes your main point of contact if you have any concerns or notice anything unusual. Your GP should have a record of your diagnosis and all the treatment you've had.

Relapsed and refractory DLBCL

Many people respond well to their first treatment for DLBCL and go into **complete remission**. However, some people need more treatment immediately after their first treatment. This might be the case if:

- the lymphoma is reduced but not completely cleared (partial remission)
- the lymphoma did not respond to treatment (refractory lymphoma).

You might also need more treatment if your lymphoma goes into remission after your first treatment, but comes back (**relapses**). Relapse is more likely to happen within 2 years of the end of your first treatment. As time goes on, lymphoma is less likely to relapse.

Treatment options for relapsed or refractory DLBCL includes:

- chemo-immunotherapy followed by a **stem cell transplant**
- **CAR T-cell therapy**
- **glofitamab**
- **loncastuximab tesirine**.

Chemo-immunotherapy and stem cell transplant

Chemo-immunotherapy for relapsed or refractory DLBCL aims to reduce the lymphoma as much as possible. This is sometimes known as 'salvage chemotherapy'. If you are fit enough, you will be considered for a stem cell transplant to increase your chance of having a long-lasting remission. A stem cell transplant works best if the lymphoma responds completely to salvage therapy, and is usually not offered otherwise.

The most commonly used salvage treatments given before a stem cell transplant include:

- **R-GDP** – rituximab with **g**emcitabine, **d**examethasone and cisplatin (also known as **Platinol®**)
- **R-DHAP** – rituximab with **d**examethasone, **h**igh-dose cytarabine (also known **Ara-C**) and cisplatin (also known as **Platinol®**)
- **R-ICE** – rituximab with ifosfamide, **c**arboplatin and **e**toposide.

Most people have a stem cell transplant using their own stem cells (**autologous stem cell transplant**). It is less common for people with relapsed and refractory DLBCL to need a stem cell transplant using donor stem cells (**allogeneic stem cell transplant**). This might be the case if

doctors are unable to collect enough of your own stem cells, or if your lymphoma relapses after an autologous stem cell transplant.

CAR T-cell therapy

If you have DLBCL that does not respond to treatment (refractory) or comes back within 12 months of initial treatment you may be offered **CAR T-cell therapy** with axicabtagene ciloleucel. This involves genetically modifying your own T cells so they can recognise and kill lymphoma cells. CAR T-cell therapy is a very intensive treatment that can cause serious side effects. It usually takes several weeks to genetically modify your T cells to make a CAR-T product. You must remain fit for treatment during this period, and most people need chemo-immunotherapy, radiotherapy or corticosteroids to keep the lymphoma under control and preserve fitness for CAR-T therapy. This is called 'bridging' therapy. The most commonly used bridging chemo-immunotherapy is polatuzumab vedotin in combination with bendamustine and rituximab. CAR T-cell therapy is only given in hospitals with the facilities and staff to treat these side effects effectively.

Glofitamab

If you have DLBCL that does not respond to treatment (refractory) or comes back after two previous systemic treatments, you may be offered **glofitamab**. Glofitamab is a type of **bispecific antibody**. Glofitamab attaches to a protein called CD20 on the surface of B cells (including the cancer cells) and to a protein called CD3 on the surface of healthy **T cells** (immune cells that can kill other cells). This helps the T cells find and destroy the lymphoma cells.

Glofitamab is given as a drip into a vein (intravenous infusion) over a few hours. To reduce the risk of side effects one dose of **obinutuzumab** is given a week before the first dose of glofitamab. Glofitamab is then started at a low dose and increased in weekly step-up doses for 3 doses. Pre-medications including steroids are also given to reduce the risk of side effects. Once at the target dose the drug is given every 3 weeks. You can have up to 12 cycles of treatment depending on response and side effects.

Loncastuximab tesirine

If you have DLBCL that does not respond to treatment (refractory) or comes back after two previous systemic treatments, including treatment with polatuzumab vedotin, you may be offered **loncastuximab tesirine**. Loncastuximab tesirine is a type of antibody therapy called an **antibody-drug conjugate**. It sticks to a protein called CD19 on the surface of B cells

(including the cancer cells) and carries the chemotherapy drug directly to them.

Loncastuximab tesirine is given as a drip into a vein (intravenous infusion) over a period of 30 minutes. You will also be given dexamethasone to help reduce side effects of treatment. You take dexamethasone either by mouth or through a drip into your vein twice a day for three days, beginning the day before you receive loncastuximab tesirine treatment.

Other treatment options

If you are not well enough for the above treatment options, you might be offered treatment with **polatuzumab vedotin** in combination with bendamustine (a chemotherapy drug) and rituximab.

You might also have radiotherapy if you have lymphoma that is causing local symptoms. This can be given before or after chemo-immunotherapy or a transplant, or instead of one of these treatments.

There are also many targeted drugs in development for DLBCL. Your doctor might suggest you take part in a **clinical trial** to give you access to a newer drug.

Research and targeted treatments

Treatment for DLBCL is usually successful but doctors continue to research treatments that are effective with as few **side effects** and **late effects** as possible. Current research is focusing particularly on targeted drugs, including:

- bispecific antibodies
- **antibody-drug conjugates**
- antibodies against CD19, CD22 and ROR1
- CAR T-cell therapies
- **checkpoint inhibitors**
- **BTK inhibitors**
- immunomodulators.

Scientists are also studying if there are any particular groups of people with DLBCL who will benefit from particular treatments, based on the biochemical or genetic profile of the lymphoma cells.

Your doctor may ask if you would like to take part in a clinical trial. Clinical trials allow new treatments to be evaluated and compared with more established treatments. Clinical trials of new treatments is the only way that new and, hopefully, better and safer treatments can become available.

Find out more about clinical trials or find a trial that might be suitable for you on [Lymphoma TrialsLink](#).

References

The full list of references for this page is available on our website. Alternatively, email publications@lymphoma-action.org.uk or call 01296 619409 if you would like a copy.

Acknowledgements

- Dr Kim Linton, Senior Lecturer and Honorary Consultant in Medical Oncology at The University of Manchester and The Christie NHS Foundation Trust.
- Dr Prem Mahendra, Consultant Haematologist, Queen Elizabeth Hospital, Birmingham.
- We would like to thank the members of our Reader Panel who gave their time to review this information.

Content last reviewed: July 2022

Updated: February 2024

Next planned review: July 2025

LYMweb0018DLBCL2022v8



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