

Grey Zone Lymphoma (GZL)

Lymphoma Australia
Nurse hotline: 1800 953 081
nurse@lymphoma.org.au

Learning about GZL is like learning a new language. It takes time and practice. Keep this information handy so you can refer back to it as you need. You can also check out our webpage [here](#)

Introduction

Grey Zone Lymphoma (GZL) is a very rare subtype of B-cell lymphoma (blood cancer) that affects both adults and children.

It is an aggressive lymphoma, which means it grows very quickly. The good news is, many aggressive lymphomas respond well to current treatments.

Because GZL is aggressive you may be cured after your treatment. Even if you are first diagnosed with the most advanced stage (stage IV), you may still be cured, or have a long-lasting remission.

What makes GZL different from other lymphomas

GZL is unique to other subtypes of lymphoma because the cancerous cells have features of both Hodgkin Lymphoma and Non-Hodgkin Lymphoma. This can make it very difficult to diagnose. Some people may even be diagnosed with Hodgkin's Lymphoma or a different type of Non-Hodgkin Lymphoma called Primary

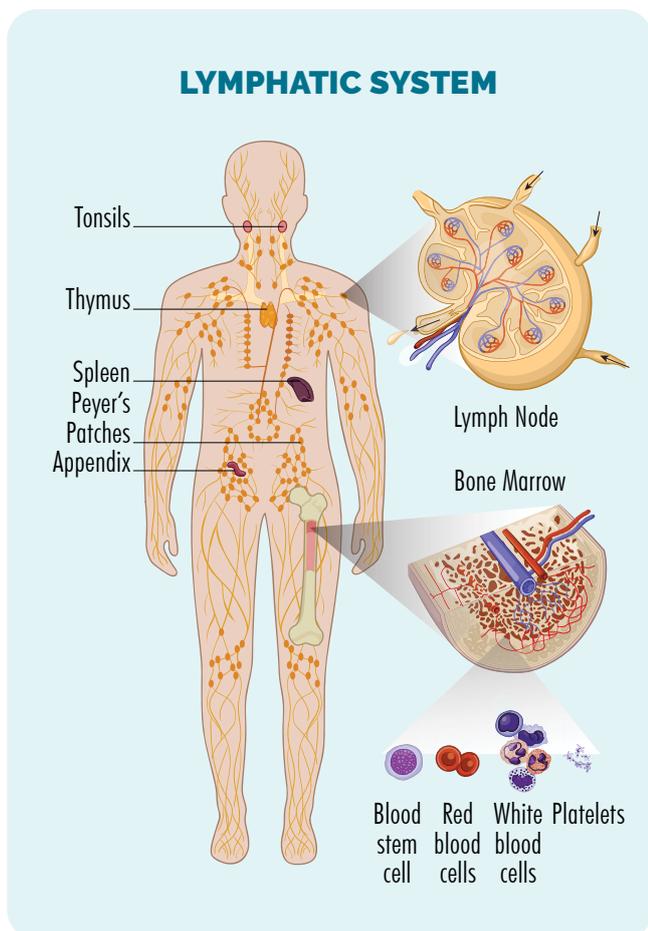
Mediastinal B-cell lymphoma (PMBCL) before they get a diagnosis of GZL.

If you have previously been diagnosed with Hodgkin's lymphoma or PMBCL and have not responded to your treatment, your doctor may want to do extra tests, or another lymph node biopsy to see if you have GZL.

What blood cells are affected in GZL?

GZL affects a type of white blood cell called B-cell lymphocytes (B-cells). B-cells are an important part of your immune system. They help to fight germs, disease and repair or destroy damaged cells. Their job is to make proteins called antibodies (also called immunoglobulins) which are matched to fight infections and disease. Each antibody can only fight one type of infection, so they are very specialised proteins of your immune system.

B-cells are made in your bone marrow (the spongy middle part of your bones), before



moving into your lymphatic system. They usually live in your lymph nodes or your spleen, but some can also be found in your thymus and blood and other parts of your lymphatic system.

They are also an important part of our immunological memory. This means that they remember infections that we have had in the past and they develop specialised cells to fight these infections or diseases if we ever get them again. Our immune system can fight off these things much quicker after we've already been infected with them.

When we have an infection

Our B cells usually live in our lymphatic system in a rested or sleeping state. They are not usually active unless they are alerted to the fact we have an infection that needs to be fought. When we have an infection, our B-cells move through our lymphatic system, and can move out of the lymphatic system to any area of our body where the infection is.

When these cells don't grow or work properly they can become cancerous lymphoma cells. Because our normal B-cell lymphocytes can be found anywhere in our body, when they become lymphoma cells, the lymphoma can also be found anywhere in your body.

Signs and symptoms of GZL

Grey Zone Lymphoma often starts in the B-cells that live in, or are passing through your thymus. You can see a picture of your thymus in the lymphatic system picture above. It is a butterfly shaped organ that is in the front of your chest just behind your breastbone. Because the cancerous cells can cause a lump or tumour to develop, they can put pressure on structures in your chest. This means that some of the symptoms you get can include:

- a dry cough
- pain, or a feeling of pressure in your chest
- difficulty breathing, wheezing or noisy breathing

- hoarseness (a rough voice)
- changes in the way one of your eyes look (due to increased pressure if one of your blood vessels is affected).

These symptoms are specific to GZL because of the location being in your chest. However, there are other symptoms that are common in all types of lymphoma. These can include:

- feeling unusually tired (fatigued)
- feeling out of breath
- bruising or bleeding more easily than usual
- infections that don't go away (refractory) or keep coming back (recurrent)
- sweating at night more than usual
- losing your appetite (not wanting to eat)
- losing weight without trying
- itchy skin
- B-symptoms.

If you are getting new or worsening symptoms, notify your doctor as soon as possible.

Diagnosis and staging

You will need a biopsy to diagnose GZL. A biopsy is a procedure to remove part or all of an affected lymph node, or a sample of your bone marrow. Once the sample is taken it is sent to pathology, where scientists check for cancerous changes to your cells. Depending on where your lymphoma is and where the biopsy is

B-SYMPTOMS

B-symptoms are a group of three distinct symptoms that some people with lymphoma can get. They often occur together and may indicate that your lymphoma is more advanced.

Contact your doctor as soon as possible if you get B-symptoms.



Drenching night sweats
– where your clothes and bedding become saturated.



Losing weight without trying,
and without other reason.



A high fever of 37.5° or more that keeps coming back or does not go away even when you don't have an infection. You may even get chills.

being taken from, you may need to have either a local or general anaesthetic. Young children will have a general anaesthetic so they sleep through and remain still during the procedure.

If your biopsy comes back positive for GZL, which means you do have this type of lymphoma, your doctor will organise more tests to see if it has spread to other parts of your body. These next tests are called staging tests. Staging refers to how far, and how many parts of your body are affected by lymphoma.

Staging tests

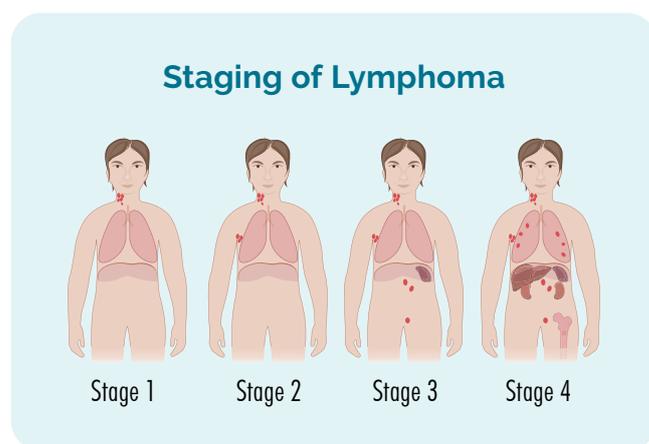
Staging tests may include:

- [Positron Emission Tomography \(PET\) scan](#)
- [Computed Tomography \(CT\) scan](#)
- [Bone Marrow Biopsy](#)
- [Lumbar Puncture](#)

You can find more information on staging tests at our website. Just look down the left-hand side to find the test you want more information on: <https://www.lymphoma.org.au/lymphoma/tests-diagnosis-and-staging/>.

Stage I (1) and II (2) GZL are considered early-stage lymphomas, meaning that only one or two areas either above OR below your diaphragm have lymphoma. Stage III (3) lymphoma is considered an advanced stage and means that you have lymphoma on both sides of your diaphragm.

Stage IV (4) lymphoma is the most advanced stage, and means you have lymphoma on both sides of your diaphragm, and in one of your organs such as your liver, lungs, brain, bones or bone marrow.



Before you start treatment

Before you start treatment you will also need to have some baseline tests done. These can include blood tests to check how well your liver and kidneys are working, scans on your heart, or lung function tests. These are to make sure that you are well enough to have treatment without it causing you to become too unwell.

Throughout your treatment you will have regular blood tests which will be compared to these baseline tests. You may also have further lung tests and heart scans to make sure that the treatment has not caused any damage to your organs.

Questions to ask your doctor - Starting treatment can feel overwhelming, and even knowing what questions to ask can be difficult. To help get you started, we have put together some questions you may like to consider asking. Click [here](#) to download our Questions to ask your Doctor" factsheet or scan the QR code at the end of this document.

Fertility – some cancer treatments can make it harder to fall pregnant, or to get somebody pregnant. If you (or your child) are planning to have children later in life, talk to your doctor about how to preserve your fertility.

Treatment

Depending on the stage of your Grey Zone Lymphoma and your overall health, including your age and any other illnesses you have, the following treatment options may be suitable for you.

First-line therapy

The first time you have treatment for GZL, it is called first-line therapy. Some of the treatments you may receive as first-line therapy are described below.

Radiation/radiotherapy

Radiotherapy is a treatment that uses high doses of radiation to kill cancer cells and shrink tumours. If you are having radiotherapy you will have a planning session before you start. This session is important so the radiation therapists

can work out how to target the radiation to your lymphoma and avoid damaging nearby healthy tissue. It is usually given every day Monday to Friday and can last between three and five weeks. You may or may not have radiation treatment with chemotherapy.

If you live far away from the radiation centre and you need help with accommodation, **talk to your doctor or nurse about what help is available to you.** You can also **contact the Cancer Council or Leukaemia Foundation in your state** to see if they can help with somewhere to stay.

Chemotherapy (chemo)

Chemotherapy are types of medications that kill fast-growing cells. Because they kill fast-growing cells, they can be very effective at treating grey zone lymphoma. Unfortunately, chemotherapy cannot tell the difference between healthy cells and lymphoma cells, so you can get unwanted side-effects from chemo. These can include hair loss, a sore mouth, nausea and vomiting, diarrhea or constipation.

Monoclonal antibody (MAB)

MABs are a type of treatment that help your own immune system to fight the lymphoma more effectively. They are given by a drip, and move through your bloodstream to the lymphoma cells and attach to these cells. By attaching to these lymphoma cells, MABs attract your own

immune cells to the lymphoma so they can begin to attack.

First-line treatment protocol

The most common first-line treatment for GZL is a treatment called DA – R-EPOCH. This treatment includes several chemotherapies and a monoclonal antibody. The medications in [DA-R-EPOCH](#) include:

- Chemotherapies – etoposide, vincristine, cyclophosphamide, and doxorubicin.
- Monoclonal antibody – rituximab.
- Steroid – prednisolone

As well as the above medications, you will have some supportive medication to help prevent or reduce side effects such as nausea and vomiting. Medication to help keep your bowels working normally is common during cancer treatment.

You may also have radiotherapy after you have had DA-R-EPOCH however, not everybody will. This will depend on the location/s and size of your disease.

Second-line therapy protocol

If your GZL does not improve with your first-line therapy (called **refractory**) or, if you respond well and the GZL goes away (you go into **remission**), but your GZL comes back (a **relapse**) you will need more treatment. Treatment after your first-line therapy is called second-line therapy – or third-line etc.

You may have more treatments similar to first-line therapy, but you may also be offered a stem-cell transplant.

Stem cell transplant

Stem Cell transplants are complex treatments that involve you having high doses of chemotherapy followed by an infusion of stem cells. Stem cells are the most immature type of blood cells, and can develop into any type of blood cell you need. The stem cells you receive may be your own stem cells, or they may come from a donor. You can learn more about stem cell transplants at <https://www.lymphoma.org.au/lymphoma/treatments/stem-cell-transplants/>.

Clinical trials

Clinical trials are an important way to find new medicines, or combinations of medicines to improve treatment or lessen side-effects. They may also offer you the opportunity to try treatment options that you would not otherwise be able to access. Without clinical trials we would not have the treatments today that we do have.

New clinical trials are starting all the time to try and find the best way to treat Grey Zone Lymphoma, while making sure you continue to have the best quality of life. If you are interested in joining a clinical trial, ask your doctor what clinical trials are available to you. You can also read our "[Understanding clinical trials](#)" fact

sheet for more information, and links to websites that you can visit to find a clinical trial yourself.

Some clinical trials for GZL currently (as of July 2022) running are looking at how the below may be used to treat people with GZL:

- CAR T-cell therapy
- Immune Checkpoint Inhibitors
- Conjugated Monoclonal Antibodies

If you are interested in learning about these treatment options, please see our webpage on treatments at <https://www.lymphoma.org.au/lymphoma/treatments/>.

Follow up when treatment ends

Finishing treatment can be a time of mixed emotions. You may feel relieved and excited, or you may feel worried and scared. You may even alternate between all of these emotions. This is very normal. However, you will not be alone. You will continue to see your specialist team on a regular basis, and be checked for any signs and symptoms of your lymphoma relapsing, and your doctor will also want to make sure you're not having any side effects from your treatment. Your doctor will let you know how often they want to see you, however the longer time you are in remission the less often they will need to see you. If you have any concerns or worries please contact your healthcare team or contact our lymphoma care

nurses on 1800 953 081. You can also email us on nurse@lymphoma.org.au.

Resources and support

Lymphoma Australia offers a wide range of resources and support for people living with lymphoma or CLL, and their carers. How to access our resources:

- **Visit** our website www.lymphoma.org.au for more information.
- **Phone** our Lymphoma Care Nurse Hotline on 1800 953 081.
- **Email** our Lymphoma Care Nurses nurse@lymphoma.org.au
- **Booklet:** Understanding Non-Hodgkin Lymphoma (NHL)
- **Downloadable information:** Visit our [website](http://www.lymphoma.org.au), or give us a call if you would like some more information on a variety topics related to lymphoma
- **Join** our Facebook page [Lymphoma Down Under](https://www.facebook.com/LymphomaDownUnder) (make sure you complete all the membership questions when you join).

Cancer Council offers a range of services, including free counselling, to support people affected by cancer, including patients, families and friends. Services may be different depending on where you live. You can contact them at www.cancer.org.au or by phone on 13 11 20.

Medicare Australia: Check with your GP if you are eligible for a Mental Health Treatment Plan (MHTP). This plan is funded by Medicare and can provide you with up to

10 sessions with a registered psychologist. More information can be found [here](#).

WeCan is an Australian supportive care website to help find the information, resources and support services you may need following a diagnosis of cancer. You can visit their website at www.wecan.org.au.

Canteen provides support for young people aged 12-25 years who have cancer, or, who have a parent with cancer. Find out more at their website here www.canteen.org.au.

Health Translations: A collection of health related information collected by the Victorian Government with resources in different languages. You can visit their website at www.healthtranslations.vic.gov.au.

Useful links

Facebook Support Group
Lymphoma Down Under



Questions to ask your
Doctor before you
start treatment



Lymphoma Australia -
Grey Zone Lymphoma
webpage



Lymphoma Australia -
Treatments



eviQ Lymphoma
Treatment Protocols



Disclaimer: Lymphoma Australia has taken every precaution to make sure the information in this document is accurate and up-to-date. However, this information is intended for educational purposes only and does not substitute for medical advice. If you have any concerns about your health or wellbeing, please contact your treating team.

2022-GZL-Snapshot