

# Grey Zone Lymphoma (GZL)

## OVERVIEW

Lymphoma is the 6th most common cancer in Australia in adult men and women. It can affect people of all ages and is the most common blood cancer. Lymphoma is a cancer of the immune system and affects lymphocytes which are a type of white blood cell. When lymphocytes gain DNA mutations they divide and grow uncontrollably resulting in lymphoma.

There are two main types of lymphocytes called B lymphocytes (B-cells) and T lymphocytes (T-cells). Lymphomas caused by B-cells are more common and account for around 85% of lymphoma cases and lymphomas caused by T-cells account for around 15% of lymphoma cases. The first lymphoma to be discovered was called "Hodgkin lymphoma" (around 15% of all B-cell lymphomas), after Thomas Hodgkin, who described it. All subsequent lymphomas discovered were called "non-Hodgkin lymphoma" (around 90% of all lymphomas, both B-cell & T-cell lymphomas).

There are over 80 different subtypes of lymphoma, that are classified according to its clinical behaviour. "Aggressive" (high grade or fast growing) lymphomas are those that grow quickly, usually weeks to months and need treatment immediately. "Indolent" (low grade or slow growing) lymphomas usually develop over years and often are not treated straight away but are monitored. It is important to know your subtype of lymphoma. Lymphoma cells can travel to any part of the body and be found in lymph nodes, the bone marrow, the spleen, blood, bone, skin and almost any organ or tissue.

Grey Zone Lymphoma (GZL) is a very rare lymphoma that has characteristics of both Hodgkin Lymphoma (HL) and Primary Mediastinal B-cell Lymphoma (PMBCL), making it very difficult to diagnose and decide upon treatment options. It is slightly more common in men than women and can occur from young adulthood through to old age.

## DIAGNOSIS AND STAGING

A biopsy is always required for a diagnosis of GZL. A biopsy is a surgical procedure to remove part of or all of an affected lymph node or other abnormal tissue to look at it under the microscope. The biopsy can be done under local or general anaesthetic depending on what part of the body is being biopsied.

GZL is more challenging to diagnose, given the similar characteristics with HL and PMBCL. It is recommended to consider a diagnosis of GZL if the biopsy results in HL but is strongly CD20 positive or a biopsy resulting in PMBCL is strongly CD15 positive. It is also highly recommended to re-biopsy a patient that has not responded to standard treatment for HL or PMBCL to look for GZL.

Once a diagnosis of GZL is made, further tests are needed to be performed to see where else in the body the lymphoma may be, otherwise referred to as the 'stage' of lymphoma (stage I-IV). Because GZL is a blood cancer it can be found anywhere in the body. Staging tests may include:

- Positron emission tomography (PET) /CT scan
- Computed tomography (CT) scan
- Bone marrow biopsy
- Lumbar puncture (if lymphoma suspected in the brain or spinal cord)

Importantly, patients with any stage of GZL are curable with standard treatments. Patients will also undergo a number of baseline tests prior to any treatment commencing to check their organ function which may include a heart scan, kidney scan, breathing tests and blood tests.

## TREATMENT OPTIONS

The standard treatment for GZL is still under consideration. Most specialists will assess whether the GZL is acting more like HL or PMBCL and give the standard treatments for these lymphomas accordingly. Treatment needs to start within a few weeks and can include:

- DA-EPOCH-R (dose adjusted etoposide, prednisolone, vincristine, cyclophosphamide, doxorubicin and rituximab)
- +/- radiotherapy
- Autologous stem cell transplant (to reduce the risk of the lymphoma coming back again)

## TREATMENTS UNDER INVESTIGATION

Many new individual and combination medicines are currently being tested in clinical trials around the world for both newly diagnosed and relapsed/refractory GZL which are being

# FACT SHEET

investigated for both HL and PMBCL:

- Bendamustine (Ribomustin™)
- Brentuximab Vedotin (Adcetris™)
- Gemcitabine (Gemzar™)
- Ibrutinib (Imbruvica™)
- Nivolumab (Opdivo™)
- Panobinostat (Farydak™)
- Pembrolizumab (Keytruda™)

## CLINICAL TRIALS

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Clinical trials are essential in identifying effective medicines and determining optimal doses of these medicines for people diagnosed with lymphoma. People who are interested in participating in a clinical trial can find one using the following methods:

1. Speak to their specialist to see what options are available
2. Go to the ClinTrial Refer website [www.clintrial.org.au](http://www.clintrial.org.au) to search available clinical trials
3. Download the ClinTrial Refer app from the Apple or Android stores for your smart phone or device. The ClinTrial Refer service was developed to connect patients, health professionals and clinical trial sites to improve access to clinical trials for patients in Australia.
4. See 'Understanding Clinical Trials' fact sheet, [www.lymphoma.org.au](http://www.lymphoma.org.au)

## FOLLOW UP

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Once treatment is completed, people with lymphoma need to be followed up by their specialist with regular appointments to monitor:

- Evaluate the effectiveness of the treatment
- Ongoing treatment side effects
- Recovery from treatment
- Signs of lymphoma relapsing
- Potential late effects caused by treatment that can occur months or years later, that can be based on the duration and frequency of treatment, age, gender and overall health of each person

## RESOURCES AND SUPPORT

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Lymphoma Australia offers a wide variety of resources and support for people with lymphoma and their carers. Please visit our website [www.lymphoma.org.au](http://www.lymphoma.org.au) for further information.

## SOME QUESTIONS TO ASK YOUR DOCTOR

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- What tests will I need to have prior to starting treatment?
- What are the treatment options for my GZL?
- How long will my treatment last?
- What will the side effects be?
- Are there any clinical trials available for me currently?
- Are there any treatment options that are better for my type of lymphoma but are yet to be funded by the PBS in Australia?