

# Marginal Zone Lymphoma (MZL)



## 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.

Marginal zone lymphomas (MZL) are a group of indolent (slow-growing) B-cell lymphomas. They account for approximately 10% of all B-cell lymphomas. The median age of diagnosis is 65 years old. It is called marginal zone because it mainly affects lymphocytes at the edges of lymphoid tissue or nodes.

## TYPES OF MARGINAL ZONE LYMPHOMA

There are three main types of MZL that include:

**Extranodal MZL or mucosa-associated lymphoid tissue (MALT)** is the most common form of MZL. It occurs outside of the lymph nodes, in places such as the stomach, small intestine, salivary gland, thyroid, eyes, and lungs. MALT lymphoma is divided into

two categories: gastric, which develops in the stomach, and non-gastric, which develops outside of the stomach. This form of lymphoma makes up about nine percent of all B-cell lymphomas. In many cases of MALT lymphoma, there is a previous medical history of inflammation or autoimmune disorders. For example, *Helicobacter pylori* (*H. pylori*), is a bacteria that is linked to stomach ulcers, and is thought to cause most cases of gastric MALT lymphoma.

**Nodal MZL** (sometimes called monocytoid B-cell lymphoma) occurs within the lymph nodes and accounts for about two percent of all B-cell lymphomas.

**Splenic MZL** occurs most often in the spleen and blood. It has been associated with Hepatitis C. This form of lymphoma makes up about one percent of all B-cell lymphomas.

## SIGNS AND SYMPTOMS

The three types of MZL can have different signs and symptoms.

**MALT** – has symptoms affecting the stomach such as indigestion, stomach pain and nausea. The symptoms of non-gastric are very variable depending on the part of the body affected.

**Nodal MZL** – The most common sign is a lump in the neck, armpit or groin or stomach. These are usually, but not always, painless and are often described as feeling "rubbery". Patients with nodal MZL may develop frequent and persistent infections.

**Splenic MZL** – The most common symptom when the spleen gets enlarged this may cause a feeling of a full stomach, even after small meals, and/or abdominal pain.

The signs and symptoms may also be similar to those people with other types of lymphoma that may include:

- Enlarged lymph nodes
- Fatigue
- Unexplained loss of weight
- Skin rash or itching of the skin
- Pains in the chest, abdomen (stomach) or bones for no obvious reason
- Fever for no known reason e.g. infection
- Drenching night sweats.

## DIAGNOSIS AND STAGING

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A biopsy is required for a diagnosis of MALT or nodal MZL. A biopsy of splenic MZL can sometimes be made if the spleen is enlarged and lymphoma cells are found in the blood and/or bone marrow. 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.

Once a diagnosis of MZL is made, further tests are needed to be performed to further clarify the subtype and to see where else in the body the lymphoma may be (or the "stage"). Staging tests include:

- Computed tomography (CT) scan
- Bone marrow biopsy
- Further blood tests

## TREATMENT OPTIONS

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MZL is a slow growing lymphoma and treatment can vary depending upon the subtype. Once treatment is completed, most patients have a period of no active disease, known as remission and may last for many years. MZL may come back, that is known as relapse and it can usually be treated again, using similar treatments as were used the first time. Many patients have a good response to treatment and long survival. The type of treatment selected for MZL depends on the stage of the disease, age, overall health, signs and symptoms of the lymphoma and the location of the disease.

Treatment Options for Gastric MALT: the initial treatment is antibiotic therapy, which is typically given for a several weeks. Approximately 70 - 90 percent of patients with evidence of *Helicobacter pylori* infection respond to antibiotic therapy, though it can take months (or even years) for the lymphoma to disappear. Approximately half of the patients require no further treatment. If the lymphoma relapses after antibiotic therapy, there are many additional treatment options available which include clinical trials, radiation therapy, chemotherapy, rituximab (a monoclonal antibody), with or without chemotherapy or even surgical excision. Your doctor will go through your options if the lymphoma relapses.

Treatment Options for Non-gastric MALT: This can appear in a variety of areas throughout the body. Therefore, treatment is usually based on the exact location and extent of spread. Treatment typically includes

- Surgery for certain sites (such as the lung or breast)
- Radiation therapy with or without chemotherapy

- Stage 3 or 4 disease Chemotherapy plus rituximab such as: bendamustine plus rituximab or R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine and prednisone)
- Not all MZL require immediate treatment and your doctor may discuss watchful waiting with you (see 'Watch and Wait' fact sheet)

Treatment Options for Nodal MZL: Because nodal MZL is most often a slow-growing disease, doctors may defer treatment until symptoms appear, an approach called "watch and wait". When treatment is necessary, options include

- Radiation therapy
- Chemotherapy
- Not all MZL require immediate treatment and your doctor may discuss watchful waiting with you (see 'Watch and Wait' factsheet)

Treatment Options for Splenic Marginal Zone Lymphoma: Several treatment options exist for splenic MZL that include:

- Splenectomy (surgical removal of the spleen)
- Low dose radiation to the spleen (for those who are not a surgical candidate)
- Rituximab (a monoclonal antibody) with or without chemotherapy

## TREATMENTS UNDER INVESTIGATION

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

- Phosphatidylinositol-3-kinase inhibitors (Umbralisib: FDA approved Jan 2019)
- B-cell receptor signalling blockers such as Ibrutinib (Imbruvica™)
- Treatments that are applicable in other B-cell lymphomas – many B-cell lymphoma trials will allow inclusion of patients with MZL

## 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 type of MZL do I have?
- What are the treatment options for my type of MZL?
- Do I need any other tests before we can decide on treatment?
- How urgent is my treatment? Do I need treatment now or could I defer until later?
- Are there any treatment options that are better for my type of lymphoma but are yet to be funded by the PBS in Australia?
- Are there any clinical trials currently available to me?

This resource was last reviewed and updated June 2019