



Hematology



Oncology

Fast Facts for Patients

Marginal Zone Lymphoma

Karger 

HEALTHCARE



First, the facts...

- 1 Marginal zone lymphoma (MZL) is a rare, slow-growing cancer of the lymphatic system that develops from a type of blood cell called a B lymphocyte.
- 2 There are three distinct types of MZL.
- 3 You may not have any symptoms of MZL when you are first diagnosed and you may not need treatment to begin with.
- 4 Although MZL cannot be cured, there are effective treatments available and some people can live with MZL for many years.
- 5 MZL may come back after treatment or may transform into an aggressive lymphoma.

This booklet aims to help you understand your disease and your options so you can talk to your healthcare team and family about your condition and its treatment. You can use the spaces on the pages to organize your notes and questions. The information in this booklet is general and if you have any concerns about your health, you should speak directly with your doctor or healthcare team.

Useful words and terms appear in bold in this booklet and as a list on page 56.

What is marginal zone lymphoma?

Lymphoma is a general name for a type of blood cancer that involves the **lymphatic system**. The lymphatic system is a network of tubes, nodes, organs, and tissues that runs throughout the body and plays a crucial role in keeping you healthy. **Marginal zone lymphoma** – often abbreviated to MZL – is a specific kind of lymphoma involving white blood cells called **B lymphocytes**. Lymphocytes are found in the lymphatic system and in the blood. You can read more about lymphocytes on page 3.

Lymphomas are divided into two groups: **Hodgkin lymphoma** and **non-Hodgkin lymphoma**. MZL is a non-Hodgkin lymphoma. There are three different types of MZL. You can read more about the types on pages 4 to 7. MZL is a **low-grade cancer**, which means it usually grows slowly. You may also hear it described as **indolent**, which also means slow growing.

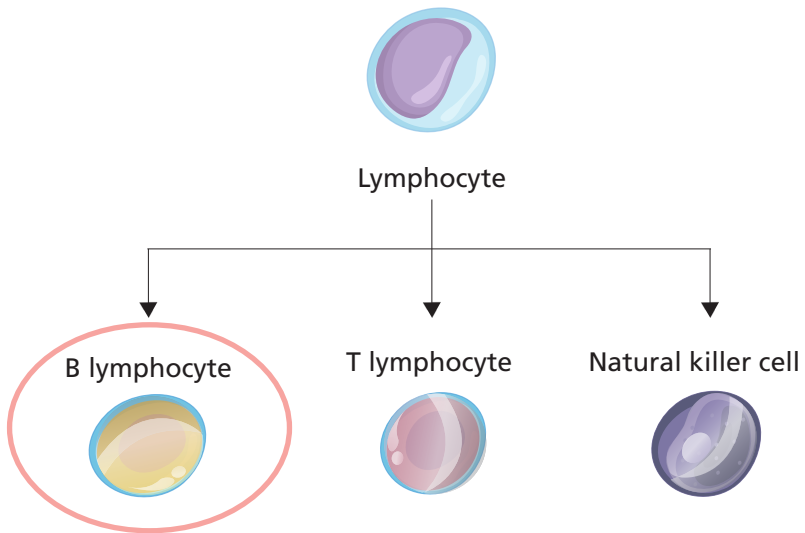
MZL can affect people of any age, but it tends to be more common in older people. The average age at diagnosis is around 70.

Widespread MZL (disease that has spread in the body) is not curable, but there are effective treatments and it's usually possible to control the disease for long periods, often for years. Some people may require ongoing or intermittent treatment to manage the disease, but many people with MZL achieve long-term **remission** and have a good quality of life.

More about lymphocytes

Lymphocytes are a type of white blood cell. They play an important role in the immune system and help to manage infection and inflammation in the body.

There are three main types of lymphocyte: **T lymphocytes**, B lymphocytes, and natural killer cells. T lymphocytes and B lymphocytes are also called **T cells** and **B cells**, and this is how they will be referred to in this booklet.



MZL is a cancer of B cells and it occurs when abnormal B cells accumulate in particular parts of the body.

B cells travel around your body in the lymphatic system. There's more information about the lymphatic system on page 6.

The three types of MZL

There are three main types of MZL:

- **mucosa-associated lymphoid tissue (MALT) lymphoma**
- **nodal MZL**
- **splenic MZL.**

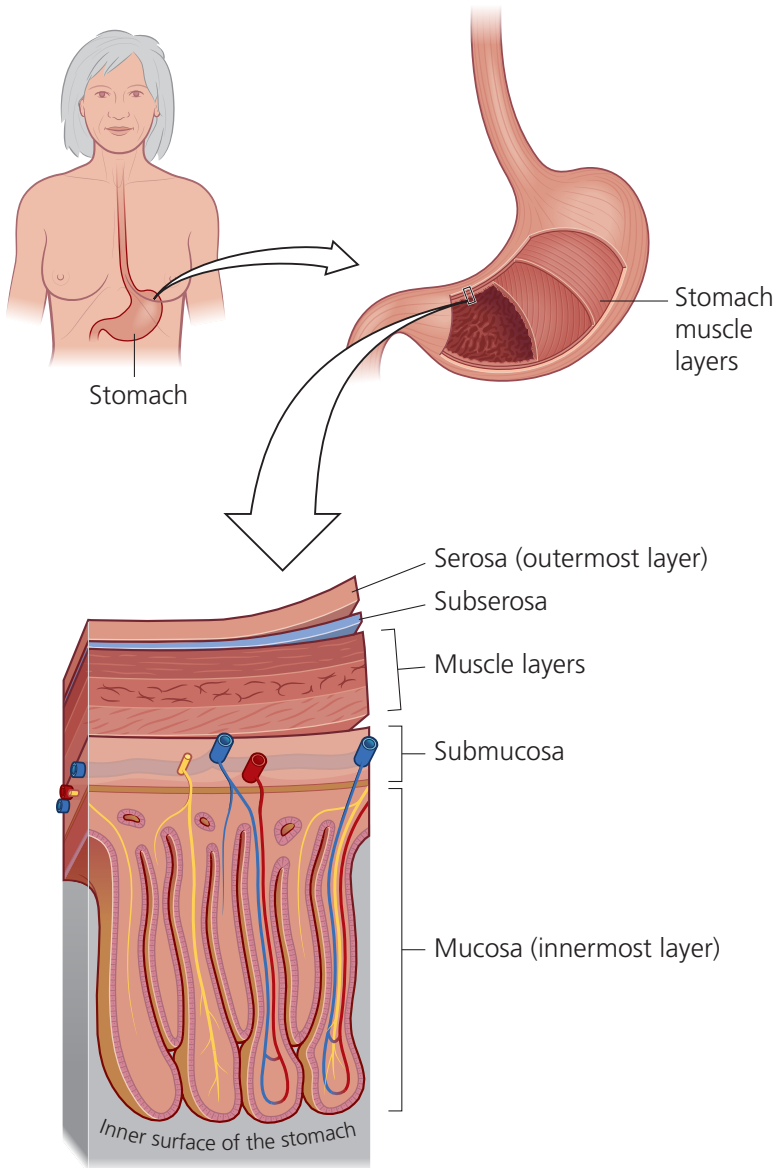
MALT lymphoma

MALT lymphoma is also known as ‘**extranodal marginal zone lymphoma** of mucosa-associated lymphoid tissue’ (EMZL). It is the most common type of MZL. About 60% of all MZL cases are this type. It is also more common in women than men: twice as many women than men are diagnosed with MALT lymphoma. **Mucosa** is a soft tissue that lines many parts of the body.

Where does MALT lymphoma occur?

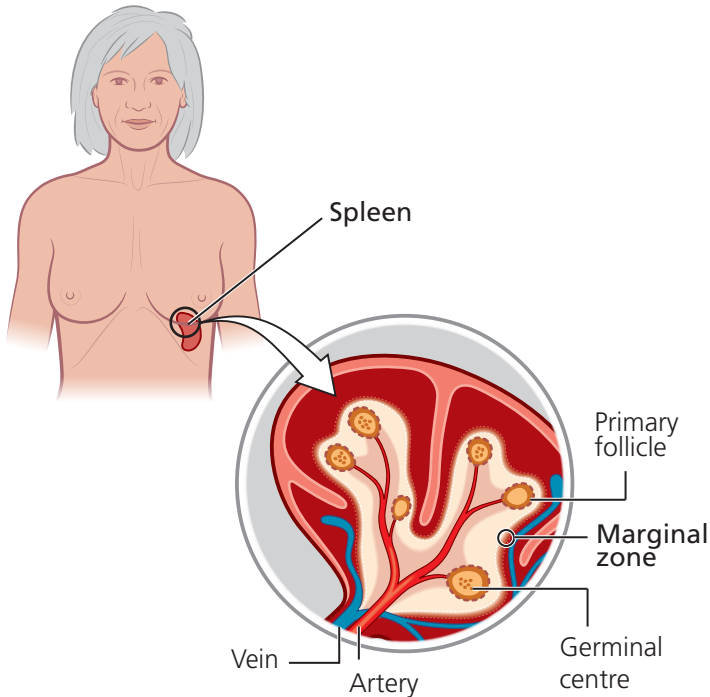
MALT lymphoma can occur in many places in the body, though the stomach is the most common. This type is called **gastric MALT lymphoma**.

Other areas of the body where MALT lymphoma can develop include the skin (where it is also known as **primary cutaneous MZL**), lungs, thyroid gland, salivary gland, bowel, and around the eye. All of these are types of **non-gastric MALT lymphoma**.



Splenic MZL

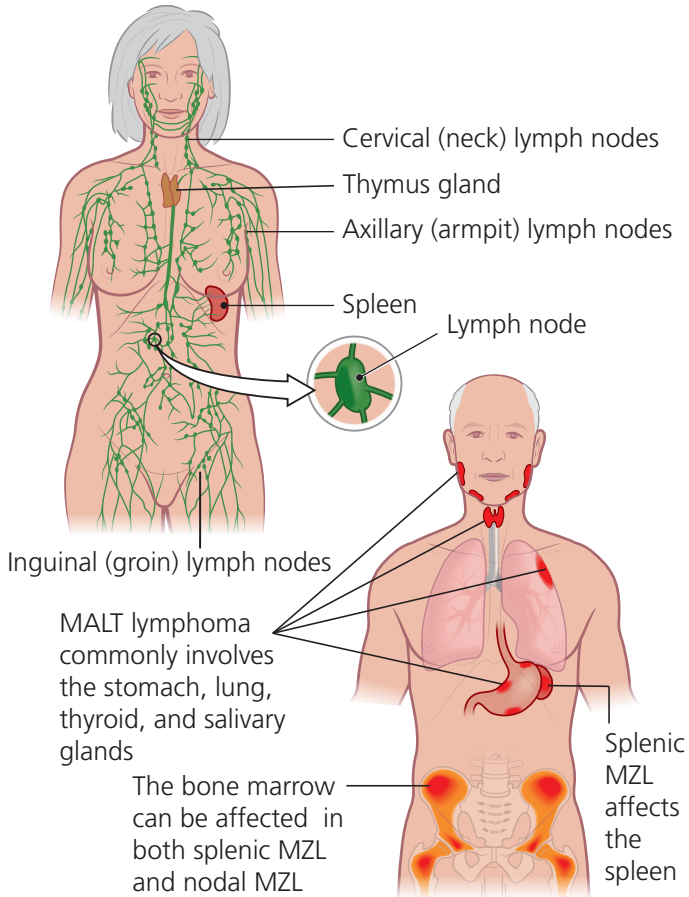
Splenic MZL is another rarer form of MZL. Somewhere between 10% and 20% of MZL is of this type. It mainly affects the **spleen**. The spleen is part of the lymphatic system and is located on the left side of the abdomen, under your ribcage (see illustration below.)



Nodal MZL

Nodal MZL is a rare form of MZL. Fewer than 10% of MZLs are of this type. It develops when the abnormal B cells build up in **lymph nodes**. Lymph nodes are small glands that are part of the lymphatic system. The lymph nodes contain follicles, which are clumps of B cells.

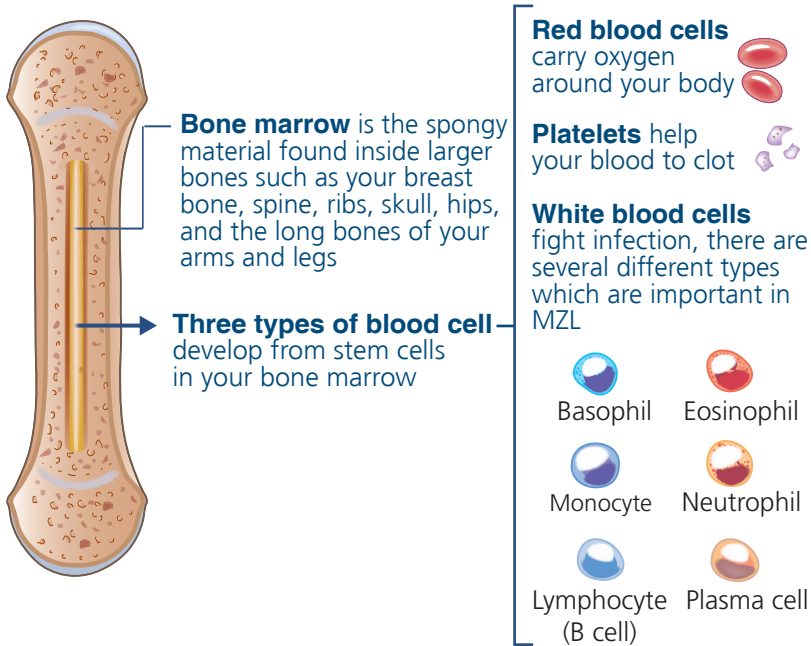
MALT lymphoma affects different parts of the body, nodal MZL affects the lymph nodes, and splenic MZL affects the spleen.



Both splenic MZL and nodal MZL can spread to the **bone marrow**. The bone marrow is found in the center of your bones and is where blood cells are made. If the bone marrow is affected by MZL, it may not be able to make enough blood cells, which can lead to problems such as **anemia**.

What is the bone marrow?

The bone marrow is where all blood cells are made. It is a spongy material found inside our bones.



When MZL spreads to the bone marrow and the spleen it can cause a number of problems, including:

- anemia leading to **fatigue** and breathlessness
- low **platelet** levels leading to blood clotting problems
- low neutrophil levels (a type of white blood cell) causing repeated infections. You can read more about how MZL might affect you on pages 11–13.

What causes MZL?

All cancers begin when changes (also called **mutations**) occur in the genes of a cell. Genes carry instructions telling normal cells how to work properly. Mutations can change the instructions and cause the cells to become abnormal, leading them to multiply in an uncontrolled way.

Mutations associated with lymphoma usually occur during your lifetime, so you cannot catch MZL from someone else, or pass it on to other people. Risk factors for MZL include getting older, as well as having a history of lymphoma in your family. In addition, **chronic** (long-term) infections and **autoimmune diseases** can prompt mutations that can lead to MZL.

Bacterial infections

Gastric MALT lymphoma is frequently linked to infection with a bacteria called ***Helicobacter pylori*** (*H. pylori*). *H. pylori* is very common, even in healthy people. It can cause stomach ulcers and indigestion but it is not usually a serious problem. However, about 9 in 10 people with gastric MALT lymphoma are infected with *H. pylori*.

Other species of bacteria that have been linked to MALT lymphoma include *Borrelia burgdorferi*, which may be linked to MALT lymphoma affecting the skin, *Campylobacter jejuni*, which may be linked to MALT lymphoma affecting the small intestine, and *Chlamydomphila psittaci*, which may be linked to MALT lymphoma affecting the area around the eye.

Hepatitis C virus infection

Long-term (chronic) infection with hepatitis C virus may increase the risk of developing splenic MZL and nodal MZL. However, most people with hepatitis C virus infection do not develop MZL.

Autoimmune diseases

Autoimmune diseases occur when the body begins to attack healthy tissues by mistake. Several autoimmune diseases may increase the risk of developing MZL.

- Sjögren's syndrome (which affects the tear and salivary glands) may increase the risk of developing MALT lymphoma and splenic MZL.
- Hashimoto's disease (which affects the thyroid gland) may increase the risk of MALT lymphoma affecting the thyroid gland.
- Rheumatoid arthritis and systemic lupus erythematosus (which can affect multiple tissues) may increase the risk of developing splenic MZL and non-gastric MALT lymphomas.

My questions

How will MZL affect me?

How MZL develops in any one person is very individual and this booklet can only give general information about the disease.

Some people will not need any treatment at first. These people may or may not have symptoms. Doctors will usually 'actively monitor' the disease in these people. You can read more about **active monitoring** on page 36.

And for those people who do need treatment, it's reassuring to know that there are a number of treatments available and more in development. Treatment options are discussed on pages 37 to 43. MZL may not be currently curable, but many people with MZL live well for a long time.

Signs and symptoms of MZL

How MZL affects you will depend on the type of MZL you have and which parts of your body it develops in.

What symptoms you experience is also very individual. Some people with MZL can have no symptoms for many years, in fact many cases of MZL are found by chance after a person is tested for another medical condition. Other people will develop symptoms quickly after diagnosis or have symptoms at the time of their diagnosis that require more urgent treatment.

"My symptoms were erratic and unpredictable. I had the classic symptoms of night sweats and weight loss 5 years before I was diagnosed. I had them for a few weeks and then they went away."

Common symptoms

In the table below you can see some of the more common symptoms for each type of MZL.

Type of MZL	Possible/common symptoms
Non-gastric MALT	
Skin	Pink, red, or purplish patches or lumps
Eye	Irritation or redness of the eye
	Lumps in the eyelid or corners of the eye
	Drooping eyelids or swelling around eyes
Bowel	Diarrhea
	Stomach pain; feeling bloated
Lung	Cough; feeling breathless
	Chest pain
Salivary glands	Lump in front of ear, or in mouth or jaw
Gastric MALT	Stomach pain; nausea
	Indigestion; feeling full
	Loss of appetite and weight loss
Splenic	Enlarged spleen, leading to anemia and fatigue
	Low platelet count causing easy bruising, easy bleeding and other symptoms; platelets help blood to clot
Nodal	Painless swelling of lymph nodes
	Anemia causing fatigue; low platelet and low white blood cell counts leading to more risk of infections
	B symptoms: night sweats, unexplained fevers, unintended weight loss (when MZL is widespread)

Other symptoms

About 50% of people with MZL have lymphoma cells in their bone marrow when they are diagnosed. When this happens, healthy blood cells are crowded out. This can lead to:

Fatigue. Not having enough healthy red blood cells causes anemia and one of the symptoms of anemia is fatigue.

Feeling breathless is another symptom of anemia. Breathlessness happens because fewer red blood cells in your body results in less oxygen reaching your muscles.

Bleeding or bruising. An increase in nosebleeds or easy bruising can be caused by not having enough platelets. The medical term for this is **thrombocytopenia**. Platelets help to clot the blood.

Infections or difficulty getting over an infection.



IMPORTANT: When you have your regular checkups, be sure to tell your healthcare team about any symptom that seems new or different.

Living with MZL

Wherever you are on your journey with MZL – recently diagnosed, starting treatment, or recuperating after treatment – eating a good diet and maintaining a healthy weight, keeping physically active, and finding ways to relieve stress and fatigue can give you a sense of control, and help you feel that you are doing the best you can for yourself.

Eat well

There's a lot of evidence that a so-called Mediterranean diet can be helpful for people with cancer. This type of diet is rich in fruit and vegetables, healthy fats such as avocado and olive oil, and fatty fish like salmon and mackerel. To minimize any inflammation in the body, you should reduce the amount of red meat you eat while ultra-processed foods and sugar should be avoided. Limiting or cutting out alcohol is also recommended.

A nutritious diet can also help increase your energy levels, support your recovery from treatment, and reduce the risk of developing new cancers and other diseases such as heart disease, diabetes, and stroke.

Challenges and finding dietary support

It isn't always easy to make changes to our diets. You may not enjoy or cannot afford the foods that are recommended. You may be cooking for other people in the family who want to eat differently. Some people live in places where accessing fresh fruit and vegetables is a challenge.

If your treatment involves chemotherapy (see page 40), you may also find that your appetite is affected or that you feel sick. Eating regular meals may be difficult. For all these reasons, you may need help to make changes to your diet.

You may be able to get help from a dietitian working with your healthcare team. A dietitian can give you specific advice and ideas for meal planning, tailored to your situation.

Many people find that their healthcare team do not give them any advice about diet. You may need to ask directly about getting help from a dietitian at the hospital or you can find an independent specialist dietitian. Patient advocacy groups can help point you in the right direction.

Supplements

You may also need to supplement with vitamins and minerals. Some vitamins may interact with some therapies, so make sure you tell your healthcare team exactly what you're taking so they can advise you.

Stay active

Regular exercise has positive effects on both the body and mind. Being physically active can help reduce cancer-related fatigue, anxiety, and depression; improve bone health, flexibility, and balance; and help you maintain a healthy weight. Many studies show that aerobic exercise – such as walking, cycling, or swimming – for just 30 minutes three or four times a week brings enormous physical and mental benefits to people living with cancer.

"I took up swimming after my treatment. I joined an adult swimming lessons group and it's been really good, very beneficial."

Getting help to navigate your exercise options

If you need help planning your exercise sessions and need advice and guidance on what exercise to do, and how often to do it, you may be able to see an exercise physiologist. Many exercise physiologists are experienced in working with people with cancer. An exercise physiologist can be especially helpful if you haven't exercised for a while and are out of condition. Some medical centers have exercise physiologists, though you may need to find one privately. Support groups in your area can be a good source of information.

Complementary therapies

Yoga, tai chi, Pilates, and meditation are all practices that people with cancer may find useful, particularly to manage stress, as are therapies such as massage, reflexology, acupuncture, and aromatherapy.

Many cancer centers now offer these kinds of complementary therapies as they can be a great help for patients during their cancer treatment. However, check with your healthcare team before having therapies like reiki and deep tissue massage as they may not be suitable for you.

"I have been having massages through my hematology team. These are with a lady specially trained to treat cancer patients. I find it extremely useful."



IMPORTANT: If you have acupuncture, always use a registered acupuncturist and preferably someone with experience of working with people with cancer. And speak to your healthcare team before starting any complementary therapy: if you have a low platelet count acupuncture may not be a suitable therapy for you.

Emotional and psychological support

Being diagnosed with cancer can be an enormous shock. It's natural to be anxious about your diagnosis and what the future might hold, about the impact on your relationship and family, and also about practical things like finances, work, and travel. If these feelings can't be managed, they can lead to depression.

One thing that people with cancer often hear is that they should 'stay positive'. Some studies have shown that having a positive attitude can lead to a better quality of life for people with cancer, but this doesn't mean that you have to put on a brave face all the time. It is normal to still feel anxious or fearful, even as you try to be positive.

Talking to family and friends

You don't need to cope with your feelings by yourself. Sharing how you feel with your family and friends may feel difficult but involving them if you can is important. Your diagnosis will affect them too and they're likely to be worried or concerned about you. They may be uncertain about how best they can help you, whether that's by offering practical support or more emotional support. They may not know how to approach the subject and instead are waiting for you to talk about it.

It may be helpful to think about what you need and let the other person know. You can reassure them that you don't expect them to have answers, but that it's helpful to have someone to listen while you talk through your concerns, or to discuss issues with them when making a decision.

Support groups

You may prefer to talk with people who are in a similar situation to you, who will understand what you are experiencing. Your healthcare team may be able to put you in touch with local face-to-face support groups or patient advocacy groups.

Online support groups

Internet (online) forums exist for many different types of cancer, so it will be easier to find other people who have MZL. Making contact online may feel less intimidating than face-to-face meetings as you can remain anonymous if you want to.

Many of the patient advocacy groups listed in Useful resources at the back of this booklet (page 55) have Facebook groups that function like forums.

"I've got a brilliant support group around me. I had no problems telling them the basics of my condition. They are very supportive."

"The lymphoma support group is great because you can share your experiences, which you can't with other people like family and friends because even though they can support you, they can't fully empathise with you."

Finding further information

It is up to you to decide how much you want to know about your cancer. You may want to hear as little as possible or you may want to learn everything you can. Not hearing certain things may mean that you dwell less on negative aspects. But learning more about MZL may give you a sense of control as you will be better placed to discuss it with your healthcare team and make decisions about your care. You may also have further questions that you'd like answered.

"When I was coming to terms with the reality of having MZL, I really didn't want lots and lots of information. But later on, during treatment, I would have loved more data."

Patient advocacy groups can be valuable sources of more information about cancer, particularly support groups for your specific cancer. If you do seek out information online yourself, be sure to check it comes from a reputable source, such as the organizations listed at the back of this booklet. And always check with your doctor that the information you've read is correct.

Effects on professional life and finances

Although MZL tends to affect older people who may be retired from work or be close to retirement, that won't be the case for everyone. You do not have to tell anyone at work about your diagnosis. However, there are laws in many countries to protect your rights at work and for this reason alone, it is a good idea to contact your human resources department as soon as you can. If your employer knows about your diagnosis, they can make what are

sometimes called ‘reasonable adjustments’. This means things like allowing you to take time off work for hospital appointments, or to alter your working hours or work from home for some of the time, or to adapt your job description.

Travel

It is possible to travel when you have MZL but you should be sensible about where you go and mindful of your risk of infection, especially if you are having treatment. Patient advocacy groups usually have up-to-date information on vaccinations and can give advice on how to prepare for a trip. If you’re receiving chemotherapy, always inform your healthcare team of your travel plans.

My notes



MZL and testing

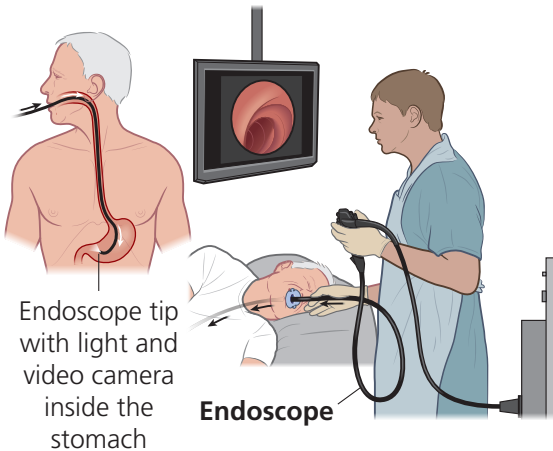
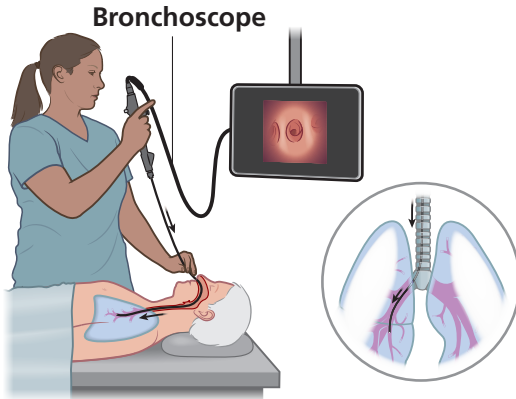
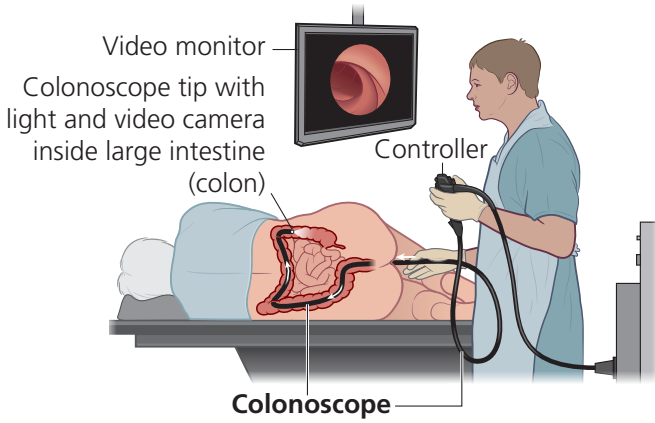
You are likely to have many different types of tests on your patient journey. Some of these tests are used to diagnose the disease and you will have had them already. Other tests are used to understand what **stage** (how **advanced** or widespread) the cancer is and its development (also called **progression**.) Some tests are used to decide if a therapy will be beneficial. You can read more about the different stages on pages 27 to 33.

The tests will vary depending on the type of MZL that you have and which parts of your body are affected.

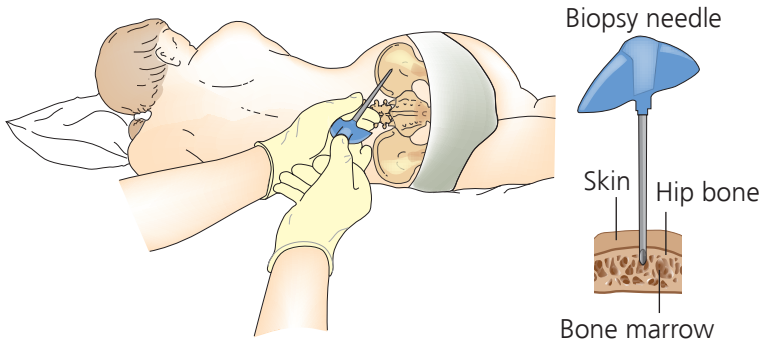
Tests to diagnose MZL

Biopsy. The diagnosis of all three types of MZL usually involves a procedure called a **biopsy**. During a biopsy, a small sample of the affected tissue is collected and then examined by a specialist **pathologist**. The pathologist will look for abnormal cells in the sample and may carry out tests to help decide which treatment might be most appropriate for you.

There are several types of biopsy. The procedure you have will depend on the type of MZL and where it occurs. If your doctor suspects you have MALT lymphoma in your stomach, lungs, or bowel you will probably have an **endoscopy**. During an endoscopy, a thin, flexible tube with a light and miniature camera are inserted into your body. Where the tube is inserted depends on which part of your body is being looked at, but you will be given a drug to relax you before the procedure. The tube also allows small surgical instruments to be passed along to collect a sample of tissue.



Bone marrow biopsy. The diagnosis of splenic MZL can be difficult, but because it can also affect the bone marrow, a **bone marrow biopsy** is often used to look for evidence of abnormal cells. The sample is usually taken from your hip bone under local anesthetic.



Core needle biopsy. To confirm a diagnosis of nodal MZL a small amount of tissue from an enlarged node is removed and analyzed under a microscope.

Tests for *H. pylori*

A breath test is often used to look for evidence of *H. pylori* infection and is very simple to do.

In cases of MALT lymphoma of the bowel, you may need to provide a poo sample (in medical terms a fecal or stool sample) that can be tested for *H. pylori*.

Blood tests

Your blood will be tested to check your general health and show how well your liver and kidneys are working. Other tests will look for signs of infection with viruses such as hepatitis C virus.

Complete blood count. A sample of your blood will also be used to check your blood cell counts. A complete blood count measures how many blood cells you have in your blood and the numbers of the different types of blood cell. For example, as explained on page 13, some types of MZL can cause anemia, which is when you have low numbers of red blood cells, or thrombocytopenia, when your platelet numbers are low.

Other blood tests. Your blood may be tested for **lactate dehydrogenase (LDH)** and **beta-2 microglobulin**.

LDH is an enzyme found in the cells of our body. Lymphoma cells can release large amounts of LDH and so it can be used as a **biomarker** of MZL if levels are high and to see how well treatment is working. Tumor biomarkers are made by cancer cells or by normal cells responding to the presence of cancer in the body. LDH levels fall or return to normal when treatment is working.

Beta-2 microglobulin is also a tumor biomarkers It can give your doctors information about how much cancer you have in your body. Beta-2 microglobulin levels often fall or return to normal when treatment is working.

Imaging

Imaging, also called radiology, includes different types of scan, including X-rays, CT scans, MRI scans, and ultrasound. These tests are done in a hospital Radiology department. You are very likely to have CT scans as this type of imaging is a very valuable tool for diagnosing, staging, and monitoring MZL.

Imaging type	Can be used to...
CT	<ul style="list-style-type: none"> • Produce pictures of your internal organs, including lymph nodes • Show where MZL has developed • Show if MZL has spread to other parts of your body • Help decide where to take a biopsy • Plan certain types of treatment • Check how well treatment is working • Show if your MZL has come back after treatment
PET-CT	<ul style="list-style-type: none"> • Help stage some cases of MZL more precisely • Check how well treatment is working • Give important information when high grade transformation is suspected (this is when the lymphoma transforms into a more aggressive form)* • Investigate for early-stage disease that is suitable for radiotherapy • Investigate suspected cases of MZL that may have become more aggressive

* 'Aggressive' means the lymphoma grows and spreads faster than a typical MZL lymphoma, which is usually slow-growing.

You may also have other scans depending on what part of your body is affected. MRI is used to scan the area around the eyes; ultrasound is used to scan the salivary glands, thyroid gland, bowel, or stomach; while an X-ray of your chest may be taken if your doctor suspects you have MALT lymphoma of the lung. Many of the patient advocacy groups we list in Useful resources at the back of the booklet will have more information on what happens during these scans and how to prepare for them.

Other tests

A sample of your MZL cells may also be used for biomarker testing. Biomarkers are characteristics of the body that can be measured. They include genes and proteins. As explained on page 9, mutations in the genes of cells can cause them to become abnormal, and mutations in B cells can be biomarkers for MZL. It is possible to detect some of these mutations which can help confirm your diagnosis and may help inform treatment decisions.

Other tests look for specific proteins on or inside your cells that are biomarkers, helping to identify the cells as B-cell lymphoma cells.

Staging your MZL

Your doctor will use your test results to stage your MZL. Staging is a description of where the cancer is, if and where it has spread, and what other parts of your body are affected. Staging helps your medical team decide whether you need treatment and to develop a treatment plan if you do.

For most types of MZL there are four stages.

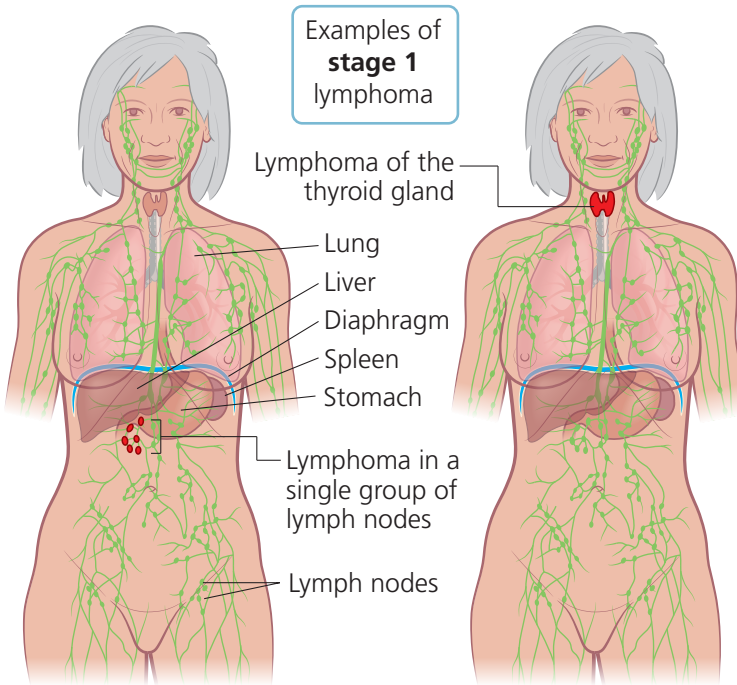
The letter E is added after the stage number if the MZL is **extranodal**. Extranodal means outside the lymph node or lymphatic organs. If you have MZL in the spleen, your doctor may use the letter S to show this.

You may also see the letters A or B as well. The letter B indicates that you also had B symptoms (night sweats, unexplained fevers, and/or weight loss) when you were tested, while the letter A indicates that you did not.

Stage 1

This means that you have **one** of the following:

- Lymphoma in a single lymph node or one group of lymph nodes, or an organ of the lymphatic system (such as the thyroid gland)
- Lymphoma in an extranodal site (1E)



Stage 1 lymphoma in a single group of lymph nodes below the diaphragm

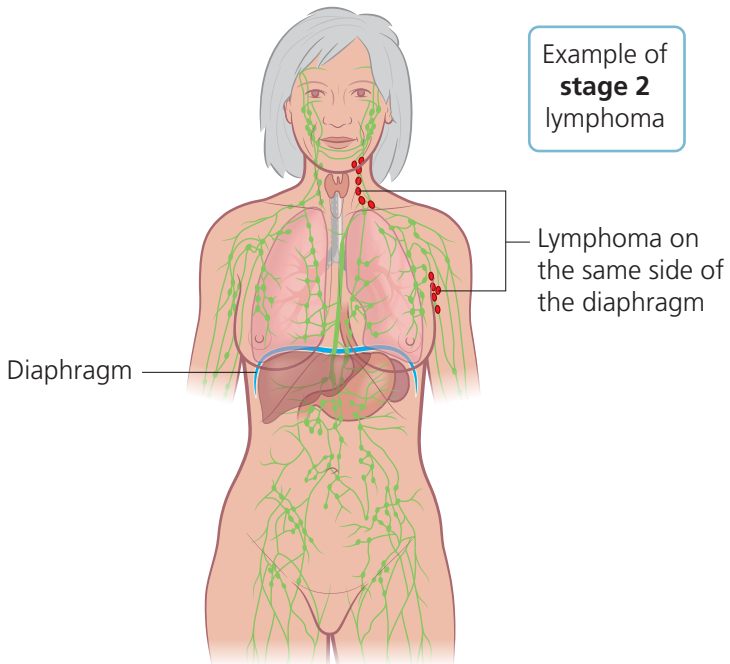
Stage 1 lymphoma in the thyroid (non-gastric MALT lymphoma)

Stage 2

This means that you have **one** of the following:

- Your lymphoma is in two or more groups of lymph nodes
- Your lymphoma is in an extranodal site and one or more groups of lymph nodes (2E)

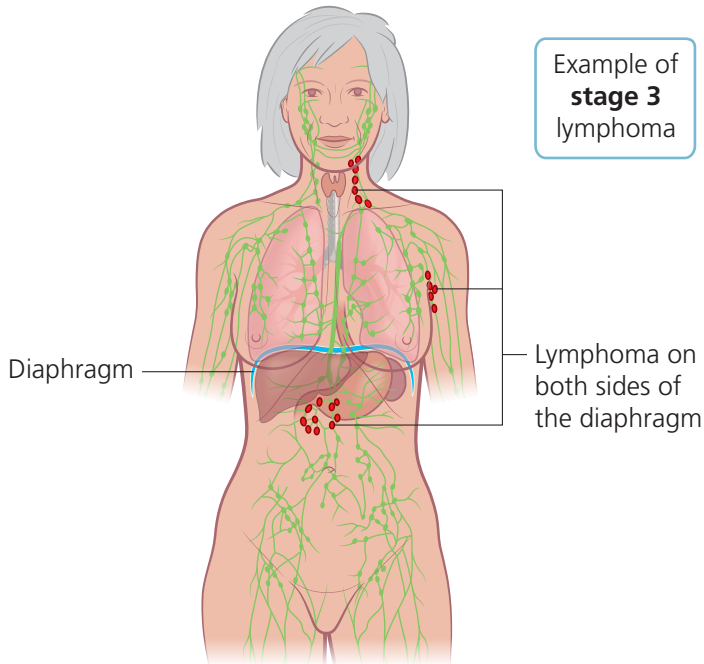
In both cases, the two sites of lymphoma are on the **same side** of the diaphragm



Stage 3

This means that you have lymphoma on **both** sides of the diaphragm:

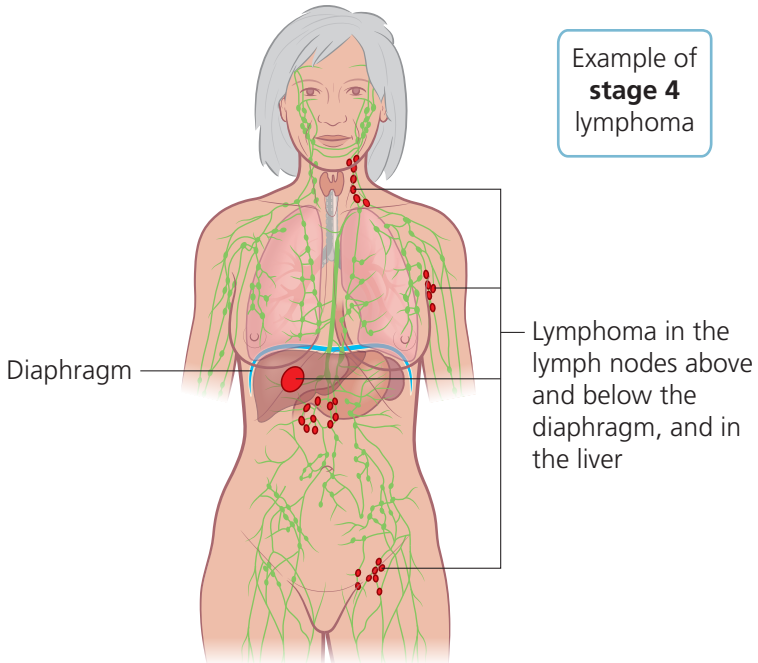
- One example (below) is that the lymphoma is in lymph nodes on both sides of the diaphragm
- Another example is that the lymphoma is in lymph nodes above the diaphragm, as well as lymphoma in the spleen



Stage 4

This means that you have **one** of the following:

- Your lymphoma is in an extranodal site and lymph nodes are affected
- Your lymphoma is in more than one extranodal site, for example the liver, bones, or lungs



Staging gastric MALT lymphoma

Another staging system called the Lugano system is also commonly used for gastric MALT lymphoma.

Lugano staging system	
Stage 1	Lymphoma is found only in the digestive tract
Stage 2	Lymphoma extends to the abdomen
Stage 2₁	Lymphoma has spread to local nodes
Stage 2₂	Lymphoma has spread to distant nodes
Stage 2E	Lymphoma has grown through the layers of the stomach wall and has spread to nearby organs and tissues
(No stage 3)	
Stage 4	Lymphoma has become widespread and is found on both sides of the diaphragm and possibly in the bone marrow or lymph nodes far away from the stomach

Types of MZL and typical stages

MALT lymphoma is often diagnosed at an early stage (stage 1 or 2). However, nodal MZL and splenic MZL are often diagnosed at an advanced stage (stage 3 or 4). In about one in three people with nodal MZL, the lymphoma cells will have spread to their bone marrow by the time they are diagnosed, while most people with splenic MZL will have lymphoma in the bone marrow too. It's important to know that there are effective treatments available for advanced stage MZL.

"I was told at the beginning, we can't cure you, but we can manage you, maybe for years."

Prognosis

A **prognosis** is an indication of how your lymphoma may progress. The term 'outlook' is also often used and means the same thing.

Your prognosis is highly individual and can vary significantly from person to person. Many factors are involved and your healthcare team may not be able to fully discuss your prognosis with you for this reason. Researchers have, however, developed a generalized way of assessing prognosis in patients with MALT lymphoma. This considers whether the patient has any of the following factors:

- Age 70 or older at diagnosis
- Stage 3 or 4 disease
- Elevated lactate dehydrogenase (LDH) levels (see page 24).

Doctors consider different factors when assessing prognosis for splenic MZL, including the age and health of the patient, blood test results such as high LDH levels or low hemoglobin (a protein in red blood cells) levels, disease stage and spread, and response to treatment. At the moment, there is no specific way of assessing prognosis for nodal MZL.

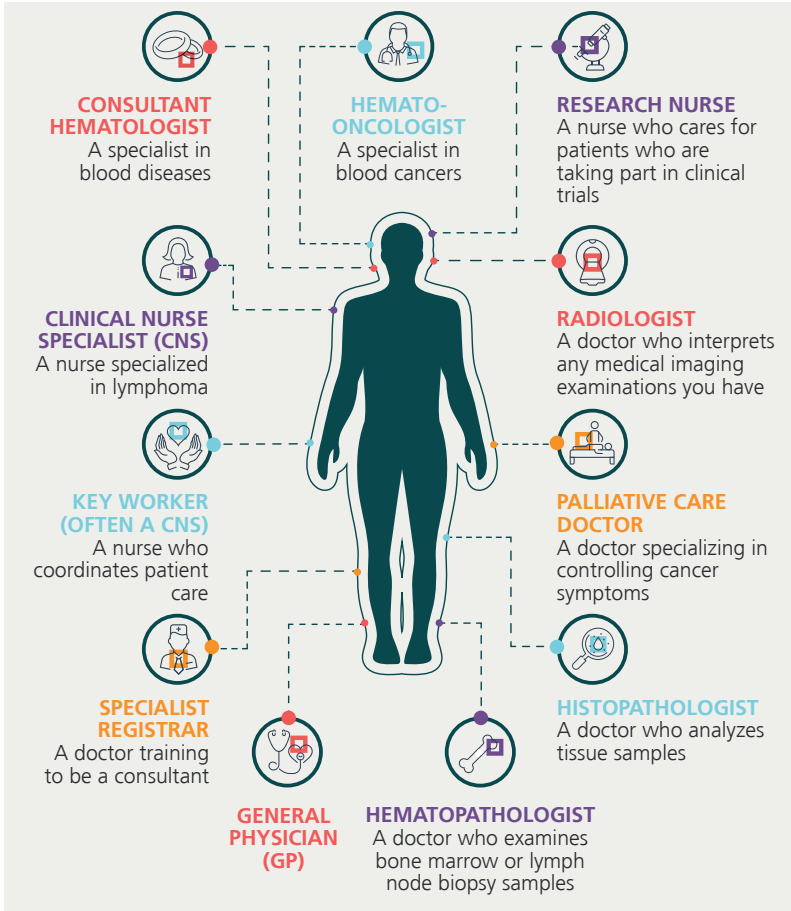
Many factors influence your prognosis, including, but not only, your test results. Your healthcare team is best placed to advise you on your outlook based on your individual circumstances.

MZL develops slowly, and treatment is often successful. New treatments are being developed all the time. However, MZL often **relapses** and needs more treatment to keep it under control.

My notes

YOUR HEALTHCARE TEAM

Your diagnosis and care is likely to involve a full team of medical professionals, all centered around **YOU** and the needs you may have throughout your journey.



You may also receive care and treatment from these **'allied healthcare professionals'**.

- DIETITIAN
- EXERCISE PHYSIOLOGIST
- COUNSELOR
- CLINICAL PSYCHOLOGIST

Treating MZL

Active monitoring

MZL is a slow-growing lymphoma and you may not need to begin treatment immediately when you are first diagnosed. If you are not showing any symptoms, or your symptoms are not serious, your doctor is likely to suggest active monitoring as the best course of action.

If you are on active monitoring, you'll have frequent appointments (typically every 3–6 months) to see your doctor and other members of your healthcare team. **It's important that you attend all the appointments.** You'll have regular examinations and tests, such as blood tests, to check for any changes and to see if your MZL is still stable. You may also have regular endoscopies if you have MALT lymphoma.

Active monitoring is also called '**watch and wait**' or '**watchful waiting**', and can last for months or even years.

It's natural to feel concerned about not being given treatment for a disease that you know you have. But all types of treatment have possible side effects, so if your MZL is not currently causing you problems, it's best to avoid these side effects for as long as you can.

It's also important to know that being on active monitoring will not affect your prognosis or how well you respond to treatment in the future.



IMPORTANT: If you are on active monitoring and you start to experience symptoms or your symptoms change, contact your healthcare team and tell them. Don't wait until your next appointment.

Starting treatment

There are currently a number of treatments that can be very effective for MZL. The treatment you receive, how often you receive it, and for how long will depend on the type of MZL you have and whether and how far it has spread in your body. Treatment aims to achieve remission of your MZL. Remission means that you have fewer or no symptoms, and fewer or no detectable signs of cancer.

Treating infections

If infection may be playing a role in your MZL you will be given treatment for the infection. This will happen even if your MZL is not causing any symptoms and you are on active monitoring.

Antibiotics are used to treat *H. pylori*. You'll also need to take medicine to reduce the amount of acid in your stomach. Treating the *H. pylori* infection can be very effective in controlling gastric MALT lymphoma associated with *H. pylori* infection. Studies have suggested that it can result in remission and long-term control of disease in three-quarters of people with early-stage gastric MALT lymphoma, although it may take up to a year after you finish taking the antibiotics before you go into remission.

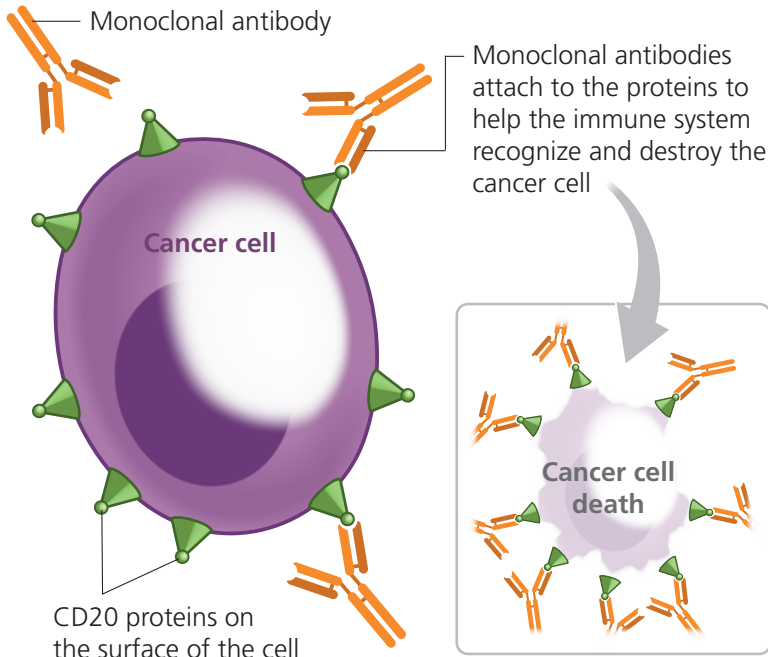
If you have other infections, such as with other types of bacteria or with hepatitis C virus, you may be treated for these first, even if you do not need immediate treatment for your MZL. It is possible that treatment for hepatitis C virus may also result in remission of some cases of MZL.

Radiotherapy

Radiotherapy is one of the most common treatments for many different types of cancer. It uses radiation to kill cancer cells such as the abnormal B cells that cause MZL. It can be used to treat gastric MALT lymphoma that does not respond to treatment for *H. pylori*, and for non-gastric MALT lymphoma and nodal MZL that are localized (not widespread) in the body. Radiation can be very effective in treating some types of MZL. Studies have shown that excellent disease control can be achieved in patients with localized MALT lymphoma, for example.

Monoclonal antibody therapies

Scientists have created antibodies in the laboratory that can be targeted against specific cancer cells. Antibodies are naturally produced by the immune system in response to bacteria, virus, or toxin. These laboratory-produced antibodies are known as **monoclonal antibodies** and they can help your immune system recognize and destroy abnormal cancer cells. Antibody therapies are **targeted therapies** because they target specific genes and proteins inside and on the surface of cancer cells. They are also called **immunotherapies** because they help stimulate your own immune system to attack the cancer cells. Depending on your MZL type, age, and fitness you may be offered treatment with monoclonal antibodies alone or in combination with chemotherapy.



Some monoclonal antibodies that are commonly used to treat MZL target a protein called CD20 that is found on the surface of B-cell lymphoma cells. This helps the immune system recognize the cells and destroy them. Some monoclonal antibodies can be used as an initial treatment for splenic MZL and used alone to treat widespread MALT lymphoma. However, they are usually combined with chemotherapy to treat other forms of MZL. This is called **chemoimmunotherapy**.

Chemoimmunotherapy, immunotherapy, and chemotherapy are all types of **systemic therapy**. This means that treatment circulates through your bloodstream to treat lymphoma wherever it is in your body.

Monoclonal antibodies can also be used as **maintenance therapy** after successful treatment with chemoimmunotherapy. You can read more about maintenance therapy on page 43.

Chemotherapy

If you are treated with chemotherapy, you will be given drugs that target rapidly dividing cells, including cancer cells. The drugs either stop the abnormal B cells from dividing so they eventually die off, or trigger mechanisms inside the cells that cause them to die.

There are lots of different chemotherapy drugs and they can be used by themselves or in combination with other chemotherapy drugs. As explained above, they are also often combined with a monoclonal antibody. More detailed information about current chemotherapy drugs and how they are combined can be found on some of the patient group websites we list in Useful resources.

Chemotherapy is not always suitable for people with MZL. This is because many are older and have other health conditions. Chemotherapy in these people can lead to unacceptable side effects.

Steroids

Steroids are widely used in the treatment of patients with cancer. They have many different uses: for example, they can be used to treat the symptoms of lymphoma and as part of a chemotherapy **regimen** to make it more effective. They can also help reduce inflammation caused by cancer treatment or reduce inflammation around a tumor that may be causing pain. They help prevent allergic reactions to some medications used to treat cancer, including monoclonal antibodies.

Splenectomy

If you have splenic MZL and your spleen becomes very enlarged (called **splenomegaly** in medical terms) your doctor may recommend that you have an operation to remove it. This operation is called a **splenectomy** and it can rapidly resolve symptoms associated with splenomegaly.

Studies show that about half of patients who undergo splenectomy do not need further treatment for splenic MZL. However, it is a major surgical procedure and there is a risk of possible complications. You will only be considered for a splenectomy if your doctor thinks you are fit enough to cope with it. Instead of splenectomy, many doctors will offer treatment with a monoclonal antibody for 6 weeks, sometimes followed by maintenance treatment with the same monoclonal antibody. This is because this treatment is easier to give and outcomes are similar to those for splenectomy.

After splenectomy. If you do have your spleen removed as part of your treatment, you will be less able to fight infections. You will need to take precautions to reduce your risk of getting an infection. These include having any vaccinations that are recommended by your healthcare team. You also usually need to take a low dose of antibiotics every day for at least two years after your surgery and possibly for the rest of your life.

Side effects of treatment

Some of the most common side effects associated with the main forms of treatment for MZL are shown in the table below. You may experience a few of them, or you may not have any at all.

If you are troubled by side effects, tell your healthcare team.

Treatment	Possible side effects
Radiotherapy	<ul style="list-style-type: none"> • Fatigue • Diarrhea • Nausea and/or vomiting • Soreness of the skin over the area treated
Chemotherapy (the side effects of chemotherapy will vary with the drugs used and the doses given)	<ul style="list-style-type: none"> • Anemia and fatigue • Nausea • Diarrhea • Hair thinning/hair loss • Increased risk of infection • Low platelet count
Monoclonal antibody therapy	<ul style="list-style-type: none"> • Flu-like symptoms, breathlessness, and rash while receiving treatment • Increased risk of infection • Anemia • Low platelet count • Headache or dizziness • Muscle or joint pain • Nausea
Steroids	<ul style="list-style-type: none"> • Indigestion • Increased appetite • Fluid buildup leading to weight gain • Changes in mood or behavior • Insomnia (difficulty sleeping)

Maintenance therapy

Although it is not used everywhere, some people with MZL receive maintenance therapy once they are in remission. Maintenance therapy aims to keep any remaining abnormal B cells under control and can help keep you in remission for longer.

Monoclonal antibody therapy is the most common maintenance therapy for MZL. Depending on the lymphoma treatment you had to achieve remission and the type of MZL, you will receive the therapy either intravenously (in a vein) or as an injection under the skin every couple of months for 1 to 2 years.

After treatment

Once you are in remission after treatment, you are likely to be put on or return to an active monitoring program (see page 36) during which you will have regular checkups and tests.

My questions

You can use this space to write questions about your treatment for your doctor

What happens if MZL comes back?

Although treatment for MZL can be very effective and can control the disease for long periods of time, it is common for all forms of MZL to come back again, even if your treatment was successful. When lymphoma comes back after achieving remission, this is called a relapse or **disease progression**. Disease progression means the lymphoma did not go away completely after the previous treatment.

While most people will have long periods of remission before they relapse, approximately 20% of patients with MZL will relapse within 2 years of their first MZL treatment. Unfortunately, studies show that MZL is harder to treat in these patients.

In some patients, treatment does not work, does not work as well as it was expected to, or their lymphoma stops responding to treatment. These people are said to have **refractory** lymphoma.

There are some other terms that you might hear too:

Complete remission: you are no longer showing any signs of lymphoma, none of your test results indicate the presence of lymphoma, and this has been the case for at least one month. Some doctors refer to this as 'no evidence of disease' (NED). However, being in complete remission is not the same as being cured. Current tests are not sensitive enough to detect every single lymphoma cell in your body and it takes only a few abnormal cells to remain after treatment for lymphoma to eventually relapse.

Partial remission: you still have evidence of lymphoma in your body but there are fewer abnormal cells and, if your MZL was widespread, fewer areas of your body are affected, and this does not change for at least one month. You may still experience symptoms of MZL.

Stable disease: your lymphoma is not changing over time. Some doctors may refer to this as ‘controlled’ or ‘no response’.

Progressive disease: your lymphoma is growing, spreading, or getting worse, and you may need to start treatment again.

Signs that your lymphoma may be relapsing

Your healthcare team should tell you what signs and symptoms may suggest your MZL is relapsing. The lymphoma might come back where it was before or it might affect a different part of your body. You might have the same symptoms as before or different symptoms. Developing B symptoms (extreme/worsening fatigue, drenching night sweats, and unexplained weight loss) is also a sign that your MZL may be relapsing.

Can I have more treatment?

The treatment you are given for relapsed or refractory MZL will depend on your age, overall health, where in your body the MZL has recurred, the symptoms you are showing, how long you were in remission for and what treatment you previously received. If you were in remission for a long time before your MZL relapsed and previous treatment was well tolerated, your doctor may decide to give you the same treatment. So, for example, if you have a relapse of gastric MALT lymphoma and you previously responded well to treatment for *H. pylori*, your doctor is likely to use the same approach again.

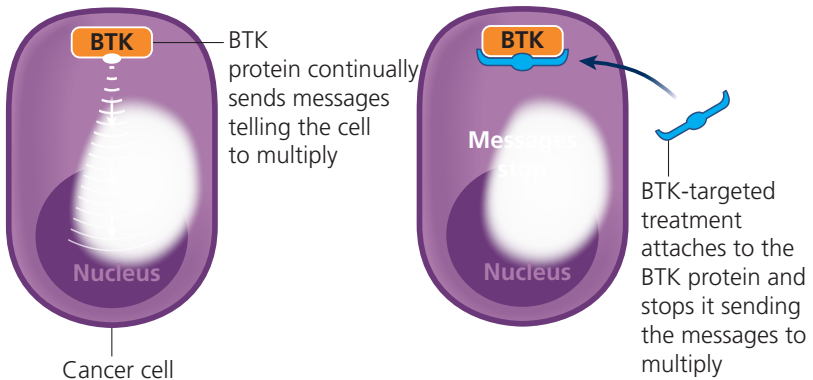
However, if you have refractory MZL, which did not respond well to the particular treatment you were given, or you experienced many side effects, then a different treatment will be used. This may be more effective than your original treatment. Your next treatment for MZL will also depend on what treatments are available at your center, including treatments in development on **clinical trials**.

My questions

Other treatments for relapsed or refractory MZL

BTK inhibitors. As explained on page 39, monoclonal antibodies are a targeted therapy for MZL. There are other types of targeted therapies available that can treat relapsed MZL, and more are under development. For example, there are drugs that target a protein called Bruton's tyrosine kinase (BTK). BTK is involved in sending signals to a cell to make it divide and it plays a key role in B cell growth.

BTK inhibitors are drugs that can block the signals sent by BTK and so can stop cells multiplying. BTK inhibitors are approved for use in the treatment of relapsed MZL in the UK, the European Union, and the USA.



Emerging therapies. BTK inhibitors are not the only new treatments being developed for MZL. Clinical trials are going on throughout the world studying different treatments and your doctor may ask if you are interested in taking part in one. You can read more about clinical trials on pages 51 to 54.

Transformation

Although MZL is generally a slow-growing cancer, in some people it can transform into a faster-growing, more aggressive, **high-grade** lymphoma. The likelihood of MZL transforming depends on the type:

- MALT lymphoma transforms in fewer than 1 in 10 people (10%)
- Nodal MZL transforms in fewer than 2 in 10 people (20%)
- Splenic MZL transforms in fewer than 2 in 10 people (20%).

The most common type of high-grade lymphoma that MZL transforms into is **diffuse large B-cell lymphoma**.

People whose MZL transforms may develop B symptoms, splenomegaly, or rapidly swelling lymph nodes. It is important that doctors differentiate between relapsing MZL and transforming MZL as they are treated differently. A PET-CT scan is usually carried out to help confirm transformation, followed by a biopsy.

What is the treatment for transformed MZL?

Doctors have not yet found the best type of treatment for transformed MZL and transformed lymphoma is usually harder to treat. Currently it is usually treated in the same way as diffuse large B-cell lymphomas and other high-grade non-Hodgkin lymphomas. This includes treatment with chemoimmunotherapy if you have not already been treated with this. Some people with transformed disease may be offered an autologous stem cell transplant if they are fit enough for this approach.

Autologous stem cell transplant

Stem cells are special cells in your body that can develop into different cell types. They also repair damaged tissue. 'Autologous' means the stem cells are collected from the patient's own body, usually the blood. Before this, the patient has a procedure called 'mobilization' that encourages the stem cells from the bone marrow to move into the bloodstream. This procedure is done before a course of high-dose chemotherapy or radiation therapy that destroys not only cancer cells but also healthy bone marrow cells. The collected stem cells are then re-infused into the patient to repopulate the bone marrow and restore its function.

My questions

Questions for your doctor about treatment for MZL may include...

What is the aim of this treatment?

How and when do I take this treatment?

For how long will I take the treatment?

Can I continue to take other prescribed drugs?

Can I continue to take vitamins and minerals?

What should I do if I forget to take a dose?

What should I do if I am sick after taking a dose?

What should I do if I have difficulty swallowing it?

What are the most common side effects of this treatment?

What can I do to manage the side effects?

How will you monitor me when I am on this treatment?

How do we know if the treatment is working?

What are the risks of this treatment for me?

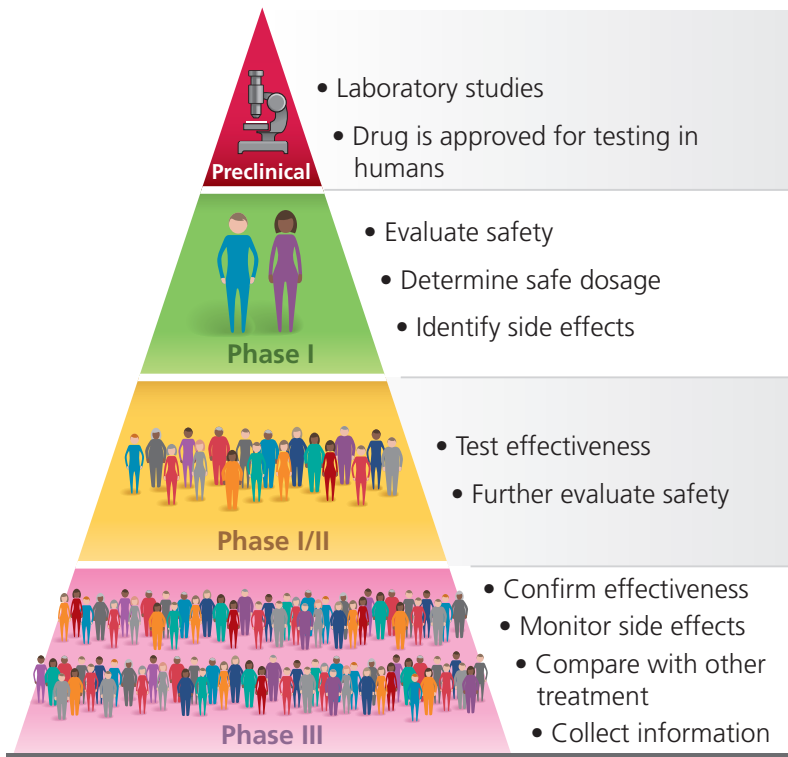
How do the outcome and side effects of this treatment compare with other treatments for MZL?

New developments in treatment

If you are interested in new treatments, you may want to find out about clinical trials.

A new treatment must go through several phases of testing before it can be proven to work better than, or as well as, existing treatment and be adopted into routine care. 'Adopted into routine care' means it can be prescribed as treatment for the condition it was tested for. A potential treatment will only move on to the next phase of research if it is safe and shows promise.

Clinical trial phases



Phase I. The first stage is to make sure a new treatment is safe. These trials are usually small, with only a few people in each one.

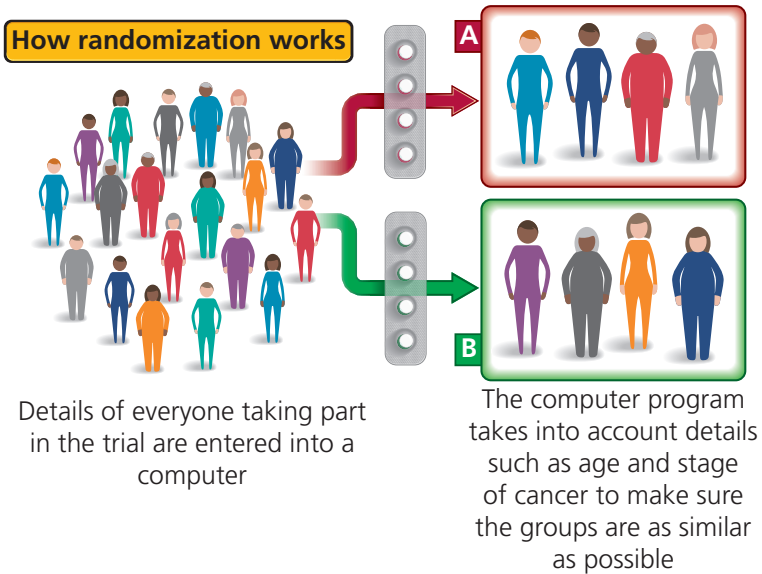
Phase II. These trials are larger. In a Phase II trial, the safety of the potential new treatment continues to be evaluated. The drug is also evaluated to see if it will be effective for a particular medical condition.

Phase III. These trials test the new treatment against the standard existing treatment to see which works best. These are the largest trials and are often international, particularly for rare conditions. Phase III trials are usually randomized.

Phase IV. These are 'real world' data collections that take place after the drug has been approved and is being prescribed.

Randomization in clinical trials

Randomization helps researchers be sure that the effects they see during a clinical trial are the result of the treatment being tested and not the result of differences between groups of people. In randomized trials, the people taking part are split into at least two groups. This is usually done by computer and aims to ensure that the groups are as similar as possible. Neither you nor the researchers can choose which group you are allocated to and you may never know which group you were in. One group of people will be given the new treatment while people in the other group will receive the existing treatment. This means that your care will not be adversely affected by taking part in the trial.



Benefits and risks of taking part in a clinical trial

People decide to take part in a clinical trial for a variety of reasons. By entering a clinical trial, you may have access to an experimental treatment and receive additional medical care and attention. You will also be helping move research forward and helping people who develop MZL in the future.

It is important to remember that if you take part in a randomized trial, you may or may not be given the experimental treatment.

Also, although experimental treatments are thoroughly tested before participants in the trial take them, there is no absolute guarantee of their safety. An experimental treatment may have side effects that were not seen in the early phases of testing when only a few people were involved in the trials.

Taking part in a clinical trial is likely to mean that you will have to have more tests or scans than usual. You may be reassured by having more checkups and tests, but you might

also find that this is stressful and has a negative impact on your wellbeing.

There will be additional time commitment involved in these extra checkups and tests and there may be costs involved too, such as the costs of travel to and from, and parking at, the treatment center. Some of these extra costs may be covered by the trial organizer and you might want to ask if any financial support is available to help you with the additional costs.

Not everyone with MZL will be able to take part in a clinical trial. Clinical trials look for participants with particular types and stages of cancer, so you may not be eligible for a current trial. You may also be ineligible because of previous treatment that you have received or other medical conditions that you have.

Finding out about clinical trials

The easiest way of finding out whether there are any clinical trials that you might be able to take part in is to check on patient advocacy sites such as Lymphoma Action and the Leukemia and Lymphoma Society. Many of the patient advocacy groups we list in Useful resources have information about current clinical trials.

Depending on where you are receiving your medical care, your doctor may also be able to tell you about a trial and whether it is suitable for you.



Useful resources

American Cancer Society
[cancer.org](https://www.cancer.org)

Blood Cancer UK
[bloodcancer.org.uk](https://www.bloodcancer.org.uk)

Cancer Research UK
[cancerresearchuk.org](https://www.cancerresearchuk.org)

Cancer Research UK database of UK cancer trials
[cancerresearchuk.org/about-cancer/find-a-clinical-trial](https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial)

Leukemia & Lymphoma Society
[lls.org](https://www.lls.org)

Leukaemia Foundation
www.leukaemia.org.au

Lymphoma Action
[lymphoma-action.org.uk](https://www.lymphoma-action.org.uk)

Lymphoma Australia
www.lymphoma.org.au

Lymphoma Research Foundation
[lymphoma.org](https://www.lymphoma.org)

Macmillan Cancer Support
[macmillan.org.uk](https://www.macmillan.org.uk)

Guide to words and phrases

Active monitoring: a period of close monitoring for signs of cancer progression in which treatment is not given; also called ‘watch and wait’ or ‘watchful waiting’.

Advanced cancer: cancer that has spread to another part of the body away from where it started. May also be known as ‘stage 4 cancer’.

Aggressive cancer: a cancer that grows quickly; may also be called a ‘high-grade cancer’.

Anemia: a condition in which the body does not have enough healthy red blood cells to carry oxygen to the tissues of the body. Anemia may be a result of splenic or nodal MZL affecting the bone marrow, or be caused by an enlarged spleen removing too many blood cells. Anemia can lead to fatigue.

Autoimmune disease: a disease in which your immune system attacks normal cells and tissues in your own body by mistake.

Beta-2 microglobulin: a tumor marker used to provide information about the amount of cancer in the body, how it might develop, and what the best treatment might be.

B cell or B lymphocyte: a type of blood cell that plays an important role in the immune system. B cells make antibodies to help fight infection.

Biomarker: a characteristic of the body that can be measured.

Biopsy: a procedure to remove a small sample of tissue for testing.

Bone marrow: soft, spongy tissue found in the center of most bones; where blood cells are made.

Bone marrow biopsy: a test where a sample of bone marrow is removed, usually from the hip bone.

B symptoms: unexplained weight loss, drenching night sweats, and fever with no obvious cause.

BTK inhibitor: a drug that inhibits the action of a protein called Bruton’s tyrosine kinase, which sends signals telling cells to divide.

Chemoimmunotherapy: combined chemotherapy and immunotherapy.

Chronic: long-lasting or persistent.

Clinical trial: a carefully designed research study to investigate a new treatment, test, medical device, or procedure.

Complete remission: there are no signs of cancer in your body and none of your test results indicate the presence of cancer.

CT: stands for ‘computed tomography’ and is a type of scan used to find where MZL is in the body.

Diffuse large B-cell lymphoma: a high-grade, aggressive lymphoma.

Endoscopy: a medical procedure that uses a tiny camera to view inside the body.

Extranodal: outside of the lymph nodes.

Extranodal marginal zone lymphoma (EMZL): another name for MALT lymphoma.

Fatigue: Extreme tiredness that makes completing many daily tasks difficult or impossible.

Gastric MALT lymphoma: MALT lymphoma developing in the mucosa lining the stomach; the most common type of MALT lymphoma.

Helicobacter pylori: a species of bacterium that is strongly associated with gastric MALT lymphoma.

High-grade cancer: a cancer that grows quickly; may also be called an 'aggressive' cancer.

Hodgkin lymphoma: one of the two main forms of lymphoma, named after the doctor who first described it.

Immunotherapy: treatments that stimulate the immune system to attack cancer cells.

Indolent cancer: a slow-growing cancer.

Lactate dehydrogenase (LDH): an indicator of tissue damage; used in staging cancer and assessing how well treatment is working.

Low-grade cancer: a slow-growing cancer.

Lymphatic system: a system of tubes, nodes, organs, and tissues that carries a fluid called lymph around the body; plays an important role in the immune system.

Lymph node: a small gland that is part of the lymphatic system.

Lymphocyte: a type of blood cell that helps fight inflammation.

Maintenance therapy: ongoing treatment to prevent cancer from returning or spreading after initial treatment.

Marginal zone lymphoma (MZL): a rare B-cell non-Hodgkin lymphoma.

Monoclonal antibody: an antibody created in a laboratory that is targeted to a particular protein or gene in a cancer cell; it helps the immune system recognize abnormal cells so they can be destroyed.

MRI: stands for 'magnetic resonance imaging'; a type of scan that may be used to detect MZL.

Mucosa: a soft tissue that lines many parts of the body, including the stomach.

Mucosa-associated lymphoid tissue (MALT) lymphoma: also called extranodal MZL; develops in tissue lining the stomach, lungs, salivary glands, thyroid, or skin, and can affect tissues around the eye.

Mutation: a change in a gene that alters the instructions telling a cell how it should work.

Nodal marginal zone lymphoma: MZL that arises in the lymph nodes of the lymphatic system.

Non-gastric MALT lymphoma: MALT lymphoma arising in tissues other than the lining of the stomach.

Non-Hodgkin lymphoma: one of the two main forms of lymphoma.

Partial remission: there is still evidence of cancer in your body, but you have fewer abnormal cells and fewer areas of your body are affected.

Pathologist: a medical professional who has undertaken specialized training to become an expert in diagnosing diseases.

PET: stands for 'positron emission tomography'; a type of scan that is often combined with CT scanning in diagnosing and staging MZL.

Phase: part of the process of a clinical trial. Phase I trials focus on safety. Phase II trials find out more about side effects and how well treatments work. Phase III trials compare the new treatment against a standard treatment to see if it works better.

Platelet: a tiny cell fragment that helps the blood to clot; also called a thrombocyte.

Primary cutaneous marginal zone lymphoma: a form of MALT lymphoma that arises in the skin.

Prognosis: an indication of how your MZL may progress.

Progression: the process through which a cancer begins to grow, spread, or get worse.

Randomization: the process of allocating participants in clinical trials to different groups.

Refractory cancer: cancer that does not respond to treatment, does not respond as well as expected, or stops responding to treatment.

Regimen: a treatment plan that sets out the schedule, duration, and dosage of treatment.

Relapse: when cancer comes back after treatment.

Remission: a significant reduction or elimination of the signs of cancer.

Spleen: an organ of the lymphatic system that plays an important role in removing old and damaged cells from the blood.

Splenectomy: surgical removal of the spleen.

Splenic marginal zone lymphoma: MZL that arises in the spleen.

Splenomegaly: enlargement of the spleen.

Splenomegaly: enlargement of the spleen.

Stable disease: cancer that is not changing over time.

Stage: how advanced a cancer is.

Systemic therapy: a treatment that circulates through the bloodstream to treat cancer wherever it occurs.

Targeted therapy: treatments that target specific genes and proteins inside and on the surface of cancer cells.

T cell or T lymphocyte: a type of blood cell that plays an important role in the immune system. T cells can either help send signals to coordinate the response of your immune system to an infection, or can directly destroy cancerous cells and cells that have been infected by viruses or bacteria.

Thrombocytopenia: a condition that results from having too few platelets in the blood. Can cause easy bleeding, or bleeding for longer, easy bruising, and a pin-point rash on the lower limbs.

Transformation: when a low-grade cancer such as MZL turns into a high-grade cancer such as diffuse large B-cell lymphoma.

Watch and wait: a period of close monitoring for signs of cancer progression in which treatment is not given; also called 'active monitoring'.

Fast Facts for Patients



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How has this book helped you? Is there anything you didn't understand?

Do you still have unanswered questions?

Please send your questions, or any other comments, to fastfacts@karger.com and help readers of future editions. Thank you!



HEALTHCARE

HEALTHCARE



Hematology



Oncology

Fast Facts for Patients Marginal Zone Lymphoma

2	What is marginal zone lymphoma?
4	The three types of MZL
9	What causes MZL?
11	How will MZL affect me?
14	Living with MZL
21	MZL and testing
27	Staging your MZL
36	Treating MZL
44	What happens if MZL comes back?
51	New developments in treatment

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Patient Information Forum

