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Marginal zone lymphoma (MZL) is a slow-growing (indolent) non-Hodgkin lymphoma (NHL). NHLs develop from lymphocytes, a type of white blood cell. In MZL, excess amounts of abnormal B lymphocytes can be found in almost any organ in the body.

Lymphatic system

The lymphatic or lymph system is a major part of the body's immune system. It is a germ-fighting network of tissues and organs that includes the bone marrow, spleen, thymus, lymph nodes, and lymphatic vessels.

Lymphatic vessels are a network of thin tubes that carry lymphatic fluid (lymph) and white blood cells into all the tissues of the body. Lymph gives cells water and food. White blood cells help fight infection and disease.

As lymph travels throughout your body, it passes through hundreds of small bean-shaped structures called lymph nodes. Lymph nodes make immune cells that help the body fight infection. They also filter the lymph fluid and remove foreign material such as bacteria and cancer cells.
Lymphocytes

Non-Hodgkin lymphoma (NHL) is a cancer of lymphocytes. A lymphocyte is a type of white blood cell. White blood cells fight infection. Lymphocytes are found in both blood and lymph tissue, as well as all organs in the body. Lymphocytes help fight and prevent infection. Lymph tissue includes lymph vessels and lymph nodes. Lymphocytes normally grow in response to infection or inflammation. When they grow on their own without proper regulation, they can develop into a lymphoma.

There are 3 main types of lymphocytes:

- **B lymphocytes or B cells** make antibodies. An antibody is a protein.
- **T lymphocytes or T cells** help fight infections, kill tumor cells, and control immune responses.
- **Natural killer (NK) cells** can kill tumor cells or virus-infected cells.

NHL can develop from either B-cell, T-cell, or NK-cell lymphocytes. Marginal zone lymphoma starts in mature B cells. B cells mature into plasma cells, which produce antibodies that are used to attack invading bacteria, viruses, and toxins. The antibody molecules latch onto and destroy invading viruses or bacteria by recruiting other components of the immune system. Cancers of plasma cells are multiple myeloma and not lymphoma.

Marginal zone lymphoma

Marginal zone lymphoma (MZL), one of the most common types of NHL, is a slow-growing type of B-cell lymphoma. MZL forms in B cells that live in the marginal zone part of the spleen, lymph nodes, or lymphoid tissues. Lymphoid or lymph tissues are organized structures that support immune responses.

The marginal zone is a very active area that receives large amounts of circulating blood. Here, blood interacts with different types of white blood cells that engulf and digest cancer cells, microbes, cellular debris, and foreign substances. When abnormal marginal zone B cells grow out of control, it can cause marginal zone lymphoma. Chronic infection, inflammation, or autoimmune disorders might cause some types of MZL due to the increased activity in the immune system. But, in many cases the cause of MZL is unknown.

MZL can be divided into 3 distinct subtypes:

- **Extranodal marginal zone lymphoma** (accounts for about 6 out of 10 MZL cases per year)
- **Nodal marginal zone lymphoma** (accounts for about 3 out of 10 MZL cases per year)
- **Splenic marginal zone lymphoma** (accounts for about 1 out of 10 MZL cases per year)

MZL has some features that overlap with another type of lymphoma called Waldenström macroglobulinemia (WM), also known as lymphoplasmacytic lymphoma (LPL). In WM, the bone marrow produces too many abnormal white blood cells that crowd out healthy blood cells.
Extranodal MZL
Extranodal marginal zone lymphoma (ENMZL) is the most common form of MZL. It occurs outside the lymph nodes (extranodal) in places such as the stomach (gastric), small intestine, salivary gland, thyroid, eyes, breast, skin, and lungs. Each type is written like this: ENMZL (gastric) or ENMZL (lung). ENMZL found in the skin is called cutaneous MZL.

In the past, the term mucosa-associated lymphoid tissue (MALT) lymphoma was used to describe this type of MZL. However, since not all sites are mucosa, such as the skin, or lymphoid, such as the stomach, ENMZL is the current, preferred term.

ENMZL can be caused by certain types of infection, inflammation, or autoimmune disorders of the affected organ. The most common location for ENMZL is the stomach, where it is often caused by the bacteria *H. pylori*. *H. pylori* can also cause stomach ulcers.

Mediterranean abdominal lymphoma or immunoproliferative small intestinal disease occurs in young adults in eastern Mediterranean countries. It often forms in the abdomen. Those with this type of ENMZL may also be infected with bacteria called Campylobacter jejuni (*C. jejuni*). Treatment options specific to this type are not covered in this book.

Nodal MZL
Nodal marginal zone lymphoma (NMZL) forms in and is mostly limited to the lymph nodes. Lymph nodes make immune cells that help the body fight infection. They also filter the lymph fluid and remove foreign material such as bacteria and cancer cells. This type of NHL is also called monocytoid B-cell lymphoma.

Splenic MZL
Splenic marginal zone lymphoma (SMZL) involves the spleen, blood, and bone marrow. The spleen makes immune cells, filters the blood, stores blood cells, and removes old blood cells. The most common sign of SMZL is an enlarged spleen. This type of MZL may be associated with hepatitis C infection, but not in all cases.
Key points

- The lymphatic or lymph system is a network of tissues and organs that helps your body fight infections and disease. It is part of the immune system.

- Non-Hodgkin lymphoma (NHL) is a cancer of the immune system that develops from lymphocytes, a type of white blood cell.

- Lymphocytes normally grow in response to infection or inflammation. When they grow on their own without proper regulation, they can develop into a lymphoma.

- Marginal zone lymphoma (MZL) starts in B cells that live in the marginal zone part of the spleen, lymph nodes, or lymphoid tissues.

- Chronic infection, inflammation, or autoimmune disorders might cause some types of MZL due to the increased activity in the immune system. But, in many cases the cause of MZL is unknown.

- Extranodal marginal zone lymphoma (ENMZL) occurs outside the lymph nodes in places such as the stomach, small intestine, salivary gland, thyroid, eyes, breast, skin, and lungs.

- Nodal marginal zone lymphoma (NMZL) forms in and is mostly limited to the lymph nodes.

- Splenic marginal zone lymphoma (SMZL) involves the spleen, blood, and bone marrow.
2

Testing for MZL

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Accurate testing is essential to confirm or diagnose and treat marginal zone lymphoma (MZL). This chapter presents an overview of possible tests you might receive and what to expect.

Test results

Results from imaging studies and biopsies will be used to determine your treatment plan. It takes many years of special training to accurately interpret these tests, so ask your care team what these test results mean. Online patient portals are a great way to find copies your test results.

Keep these things in mind:

- Choose a friend, family member, or peer who can drive you to appointments, provide meals, or offer emotional support during diagnosis and treatment. Bring someone with you to doctor visits, if possible.
- Write down questions and take notes during appointments. Don’t be afraid to ask your care team questions. Get to know your care team and help them get to know you.
- Get copies of blood tests, imaging results, and reports about the specific type of cancer you have.
- Organize your papers. Create files for insurance forms, medical records, and test results. You can do the same on your computer.
- Keep a list of contact information for everyone on your care team. Add it

Create a medical binder

A medical binder or notebook is a great way to organize all of your records in one place.

- Make copies of blood tests, imaging results, and reports about your specific type of cancer. It will be helpful when getting a second opinion.
- Choose a binder that meets your needs. Consider a zipper pocket to include a pen, small calendar, and insurance cards.
- Create folders for insurance forms, medical records, and tests results. You can do the same on your computer.
- Use online patient portals to view your test results and other records. Download or print the records to add to your binder.
- Organize your binder in a way that works for you. Add a section for questions and to take notes.
- Bring your medical binder to appointments. You never know when you might need it!
to your phone. Hang the list on your refrigerator or keep it in a place where someone can access it in an emergency. Keep your primary care physician (PCP) informed of changes to this list. You are encouraged to keep your PCP. They are great partners in your care.

- Include in your contact list information your exact subtype of MZL, as well as any treatment and the date it started.

General health tests

Medical history
A medical history is a record of all health issues and treatments you have had in your life. Be prepared to list any illness or injury and when it happened. Bring a list of old and new medicines and any over-the-counter medicines, herbs, or supplements you take. Some supplements interact and affect prescriptions that your doctor may give you. Tell your doctor about any symptoms you have. A medical history, sometimes called a health history, will help determine which treatment is best for you.

Family history
Some cancers and other diseases can run in families. Your doctor will ask about the health history of family members who are blood relatives. This information is called a family history. Ask family members on both sides of your family about their health issues like heart disease, cancer, and diabetes, and at what age they were diagnosed. It is important to know the specific type of cancer, or where the cancer started, and if it is in multiple locations. It is unusual for MZL to run in families.

Physical exam
During a physical exam, your health care provider may:

- Check your temperature, blood pressure, pulse, and breathing rate
- Check your height and weight
- Listen to your lungs and heart
- Look at your skin and eyes and in your ears, nose, and throat
- Feel and apply pressure to parts of your body to see if organs are of normal size, are soft or hard, or cause pain when touched. Tell your doctor if you feel pain.
- Feel for enlarged lymph nodes in your neck, underarm, and groin. Tell your doctor if you have felt any lumps or have any pain.
Fertility (all sexes)

Treatment such as chemotherapy can affect your fertility, the ability to have children. If you think you want children in the future, ask your doctor how cancer and cancer treatment might change your fertility. In order to preserve your fertility, you may need to take action before starting cancer treatment. Those who want to have children in the future should be referred to a fertility specialist to discuss the options before starting treatment.

Fertility preservation is all about keeping your options open, whether you know you want to have children later in life or aren’t really sure at the moment. Fertility and reproductive specialists can help you sort through what may be best for your situation.

More information on fertility preservation can be found in the NCCN Guidelines for Patients: Adolescents and Young Adults with Cancer, available at NCCN.org/patientguidelines.

Impaired fertility

Treatment might cause your fertility to be temporarily impaired or interrupted. This temporary loss of fertility is related to your age at time of diagnosis, treatment type(s), treatment dose, and treatment length. Talk to your doctor about your concerns and if you are planning a pregnancy.

Preventing pregnancy

Preventing pregnancy during treatment is important. Cancer and cancer treatment can affect the ovaries and damage sperm. Hormonal birth control may or may not be recommended, so ask your doctor about options such as intrauterine devices (IUDs) and barrier methods. Types of barrier methods include condoms, diaphragms, cervical caps, and the contraceptive sponge.

Those with ovaries

Those who can become pregnant will have a pregnancy test before starting treatment. Cancer treatment can hurt the baby if you are or become pregnant during treatment. Therefore, birth control to prevent pregnancy during and after treatment is recommended. If you are pregnant or breastfeeding at the time of your cancer diagnosis, certain treatments will need to be avoided.

Menstruation, menses, menstrual flow, or your “period” may stop during treatment, but often returns within 2 years after treatment in those 40 years of age and under. It is still possible to become pregnant even though you might not have a period. Therefore, birth control is recommended during and after treatment. Consult your doctor for the best time to plan a pregnancy.

Those with testicles

Cancer and cancer treatment can damage sperm. Therefore, use contraception (birth control) such as condoms to prevent pregnancy during and immediately after cancer treatment.
Performance status

Performance status (PS) is a person’s general level of fitness and ability to perform daily tasks. Your state of general health will be rated using a PS scale called ECOG (Eastern Cooperative Oncology Group). PS is one factor taken into consideration when choosing a treatment plan. Your preferences about treatment are always important.

The ECOG PS scores range from 0 to 5.

- PS 0 means the person is fully active.
- PS 1 means the person is still able to perform light to moderate activity, but with some limitations.
- PS 2 means the person is limited to the chair or bed less than half of the time and still able to care for self.
- PS 3 means the person is limited to the chair or bed more than half of the time.
- PS 4 means the person is totally confined to the bed or chair and completely disabled.
- PS 5 means the person is not alive.

Good PS is usually PS 0 or PS 1.

Blood tests

Blood tests check for signs of disease and how well organs are working. They require a sample of your blood, which is removed through a needle placed into your vein.

Be prepared to have many blood tests. You might have blood tests as often as every 6 to 48 hours during MZL treatment and recovery to check treatment results, blood counts, and the health of organs like your liver and kidneys.

Some possible tests described next are listed alphabetically and not in order of importance.

Complete blood count

A complete blood count (CBC) measures the levels of red blood cells (RBCs), white blood cells (WBCs), and platelets (PLTs) in your blood. Your doctor will want to know if you have enough RBCs to carry oxygen throughout your body, WBCs to fight infection, and PLTs to control bleeding. Your blood gives a picture of your overall health.

Comprehensive metabolic panel

A comprehensive metabolic panel (CMP) measures 14 different substances in your blood. It is usually done on the plasma part of your blood. A CMP provides important information about how well your kidneys and liver are working, among other things.

Creatinine

Creatinine is a waste produced in the muscles. Every person generates a fixed amount of creatinine every day based on how much muscle they have. It is filtered out of the blood by the kidneys. The level of creatinine in the blood tells how well the kidneys are working.
Higher levels of creatinine mean the kidneys aren’t working as well as they were when someone had lower levels of creatinine.

**Differential**
There are 5 types of WBCs: neutrophils, lymphocytes, monocytes, eosinophils, and basophils. A differential counts the number of each type of WBC. It also checks if the counts are in balance with each other.

**Electrolytes**
Electrolytes help move nutrients into cells and help move waste out of cells. Electrolytes are ions or particles with electrical charges that help the nerves, muscles, heart, and brain work as they should. Your body needs electrolytes to function properly.

**Helicobacter pylori**
_Helicobacter pylori_ or _H. pylori_ is a type of bacterium that causes inflammation and ulcers in the stomach or small intestine. People with _H. pylori_ infections may be more likely to develop cancer in the stomach, including extranodal marginal zone lymphoma (ENMZL).

**Hepatitis B and C**
Hepatitis is a virus that causes inflammation of the liver. Hepatitis B (HBV) and hepatitis C (HCV) are spread by contact with blood and other bodily fluids. A blood test will show if you had hepatitis in the past or if you have it today. Some treatments might cause HBV to reactivate, which can cause liver damage. It’s important to let your doctor know if you have ever been infected with HBV.

**HIV**
Human immunodeficiency virus (HIV) causes acquired immunodeficiency syndrome (AIDS). An HIV antibody test checks for HIV antibodies in a sample of blood, urine, or saliva. It’s important to let your doctor know if you have ever been infected with HIV.

**HLA typing**
Human leukocyte antigens (HLAs) are proteins found on the surface of most cells. They play an important role in your body’s immune response. HLAs are unique to each person. They mark your body’s cells. Your body detects these markers to tell which cells are yours. In other words, all your cells have the same set of HLAs. Each person’s set of HLAs is called the HLA type or tissue type.

HLA typing is a blood test that detects a person’s HLA type. This test is done before a donor (allogeneic) stem cell transplant. To find a donor match, your proteins will be compared to the donor’s proteins to see how many proteins are the same. A very good match is needed for a transplant to be a treatment option. Otherwise, your body will reject the donor cells or the donor cells will react against your body. Blood or tissue samples from you and your blood relatives will be tested first.

**Immunofixation**
An immunofixation (IFE) blood test measures certain proteins in the blood. Proteins play many important roles, including providing energy for the body, rebuilding muscles, and supporting the immune system.
Immunoglobulins
Quantitative immunoglobulins measure the amount of immunoglobulins, also known as antibodies, in your blood. Antibodies are proteins made by the immune system. An immunoglobulin test usually measures three specific types of immunoglobulins. They are called IgG, IgM, and IgA.

Infections related to MZL
Certain infections can cause on-going (chronic) inflammation and increased activity of the immune system. Infections such as Helicobacter pylori (H. pylori), Chlamydia psittaci (C. psittaci), Campylobacter jejuni (C. jejuni), Borrelia burgdorferi (B. burgdorferi), and hepatitis C virus (HCV) have been found in those with MZL. These infections are different from infections that can be a result of treatment found in the supportive care section of Chapter 3.

Lactate dehydrogenase
Lactate dehydrogenase (LDH) or lactic acid dehydrogenase is a protein found in most cells. Dying cells release LDH into blood. Fast-growing cells also release LDH.

Pregnancy test
If planned treatment might affect pregnancy, then those who can become pregnant will be given a pregnancy test before treatment begins.

SPEP
Serum protein electrophoresis (SPEP) examines specific proteins in the blood called globulins, which may be increased in certain conditions.
Biopsy

A biopsy is the removal of a sample of tissue or fluid for testing. It is an important part of an accurate diagnosis of lymphoma. Your sample should be reviewed by a pathologist who is an expert in the diagnosis of MZL. The pathologist will note the overall appearance and the size, shape, and type of your cells. This review is often referred to as histology, histopathology, or hematopathology review. Tests will be done on the biopsied cells. Ask questions about your biopsy results and what it means for your treatment.

Types of possible biopsies include:

- **Fine-needle aspiration (FNA) and core biopsy (CB)** use needles of different sizes to remove a sample of tissue or fluid.
- **Incisional biopsy** removes a small amount of tissue through a cut in the skin or body.
- **Excisional biopsy** removes the entire tumor through a cut in the skin or body.
- **Lymph node biopsy** removes tissue from a lymph node.
- **Endoscopic biopsy** uses a thin, tube-shaped tool guided through the mouth to take a sample of the stomach.

A biopsy is usually done with other lab methods in order to accurately diagnose the type of MZL. Core or excisional biopsies are often preferred for diagnosing MZL.

These methods include

- Immunohistochemistry (IHC)
- Flow cytometry
Testing for MZL Biopsy

Biomarker testing to detect gene rearrangements and karyotype or fluorescence in situ hybridization (FISH) for major translocations

In a gene rearrangement, there is either loss or gain of chromosomal material. A translocation refers to the transfer of genetic material from one chromosome to another.

Lymph node biopsy

A lymph node biopsy is recommended to diagnose MZL. Lymph nodes are usually too small to be seen or felt. Sometimes, lymph nodes can feel swollen, enlarged, hard to the touch, or don’t move when pushed (fixed or immobile). A lymph node biopsy can be done using a needle biopsy procedure or as a small surgery to remove (excise) a lymph node.

Bone marrow tests

Bone marrow tests might be done in certain cases.

There are 2 types of bone marrow tests that are often done at the same time:

- Bone marrow aspirate
- Bone marrow biopsy

Your bone marrow is like a sponge holding liquid and cells. An aspirate takes some of the liquid and cells out of the sponge, and a biopsy takes a piece of the sponge.

The samples are usually taken from the back of the hip bone (pelvis). You will likely lie on your belly or side. Your doctors will first clean and give sedation or numb your skin and outer surface of your bone. For an aspirate, a hollow needle will be pushed through your

What is your family health history?

Some cancers and other diseases run in families—those who are related to you through genes passed down from parent to child. This information is called a family health history. You can ask family members about their health issues like heart disease, cancer, and diabetes, and at what age they were diagnosed. For relatives who have died, ask about the cause and age of death.

Start by asking your parents, siblings, and children. Next, talk to half-siblings, aunts and uncles, nieces and nephews, grandparents, and grandchildren.

Write down what you learn about your family health history and share this information with your health care provider.

Some of the questions to ask include:

- Do you have any chronic diseases, such as heart disease or diabetes, or health conditions such as high blood pressure or high cholesterol?
- Have you had any other diseases, such as cancer or stroke?
- How old were you when each of these diseases and health conditions was diagnosed?
- What is our family’s ancestry—from what countries did our ancestors originate?
Testing for MZL Biomarker tests

Inside our cells are deoxyribonucleic acid (DNA) molecules. These molecules are tightly packaged into what is called a chromosome. Chromosomes contain most of the genetic information in a cell. Normal human cells contain 23 pairs of chromosomes for a total of 46 chromosomes. Each chromosome contains thousands of genes. Genes are coded instructions for the proteins your cells make. A mutation is when something goes wrong in the genetic code.

A sample from your biopsy may undergo lab tests to look for specific DNA mutations/alterations, protein levels, or other molecular features. This information is used to learn more about your subtype of MZL. It is sometimes called molecular testing, tumor profiling, gene expression profiling, or genomic testing.

Biomarker testing includes tests of genes or their products (proteins). It identifies the presence or absence of mutations and certain proteins that might suggest the lymphoma subtype, assess prognosis, and guide treatment. Proteins are written like this: BCL6. Genes are written with italics like this: BCL6.

Deletions
When part of a chromosome is missing, it is called a deletion. For example, in del(7q) the “q” part of chromosome 7 is missing (deleted). Specific chromosomal deletions can be found in some types of marginal zone lymphomas, but can also be found in other types of blood cancers and disorders.

FISH
Fluorescence in situ hybridization (FISH) is a method that involves special dyes called probes that attach to pieces of DNA. Since this test doesn’t need growing cells, it can be performed on either bone marrow, a lymph node, or blood sample.

FISH can find translocations that are too small to be seen with other methods. A translocation occurs when parts of two chromosomes switch with one another. However, FISH can only be used for known changes. It cannot detect all the possible changes found with a karyotype.

Gene rearrangements
In gene rearrangements, part of a gene has broken off and attached to another gene, creating a new gene. When one cell divides many times, the entire group of cells is called clonal or clonality. In clonal rearrangements, abnormal groups are found.

Karyotype
A karyotype is a picture of chromosomes. Normal human cells contain 23 pairs of chromosomes for a total of 46 chromosomes. A karyotype will show extra, missing, rearranged, or abnormal pieces of chromosomes. Since a karyotype requires growing cells, a sample of bone marrow or blood must be used.
**Mutation testing**
A sample of your blood or bone marrow will be used to see if the MZL cancer cells have any specific mutations. Some mutations can be targeted with specific therapies. This is separate from the genetic testing for mutations that you may have inherited from your parents.

Mutation testing includes tests of genes or their products (proteins). Subtle new drug-resistant mutations may occur over time. Mutations can also happen during treatment. Mutation testing is used to look for these new mutations. Some mutations lead to resistance to certain targeted therapies. There are many possible mutations.

**Translocations**
Translocation is a switching of parts between two chromosomes. A translocation between chromosome 11 and 18 is written as t(11;18). Specific translocations can help distinguish between types of blood cancers and disorders.

**Comparative genomic hybridization**
Comparative genomic hybridization (CGH) is a technique that compares DNA samples from normal tissue and tumor tissue. It is used to detect abnormal chromosomes.

**High-throughput sequencing**
High-throughput sequencing (HTS) is capable of sequencing hundreds of millions of DNA molecules at a time.

**Next-generation sequencing**
Next-generation sequencing (NGS) is a high-throughput method used to determine a portion of a person’s DNA sequence.

**PCR**
A polymerase chain reaction (PCR) is a lab process that can make millions or billions of copies of your DNA (genetic information) in just a few hours, but results can take days. PCR is very sensitive. It can find 1 abnormal cell among more than 100,000 normal cells. These copies, called PCR product, might be used for HTS or NGS.

**Genetic testing**
Genetic testing is done using blood or saliva (spitting into a cup). The goal is to look for gene mutations inherited from your biological parents called germline mutations. Some mutations can put you at risk for more than one type of cancer. You can pass these genes on to your children. Also, family members might carry these mutations. Tell your doctor if there is a family history of cancer.

There are 3 major types of genetic testing:

- **Cytogenetic** - to examine whole chromosomes
- **Biochemical** - to measure proteins produced by genes
- **Molecular** - to look for small DNA or gene mutations

While it can be confusing, just know that testing done to look for an inherited gene mutation or an inherited risk of cancer is
different than genetic testing done on cancer cells or testing to look for proteins produced by cancer cells. This book refers to tests done on cancer cells or to look for evidence of cancer as biomarker tests.

**Immunophenotyping**

Immunophenotyping is a process that uses antibodies to detect the presence or absence of certain antigens. Antigens are proteins or markers that can be found on the surface of or inside all cells, including white blood cells. Specific groupings of antigens are normal. However, some specific patterns of antigens called the immunophenotype are found on abnormal cells including non-Hodgkin lymphoma (NHL) and MZL.

Immunophenotyping can be done using specialized techniques called flow cytometry or immunohistochemistry. These techniques are used to distinguish MZL from other types of lymphoma. Immunophenotype can change as cancer progresses. MLZ immunophenotype is usually CD10-, CD5-, CD20+, cyclin D1-, BCL2- follicles. Additional markers are used to establish subtype.

**Flow cytometry**

Flow cytometry is a laboratory method used to detect, identify, and count specific cells. Flow cytometry involves adding a light-sensitive dye to cells. The dyed cells are passed through a beam of light in a machine. The machine measures the number of cells, things like the size and shape of the cells, and proteins on the surface of thousands of cells. Flow cytometry may be used on cells from circulating (peripheral) blood, bone marrow, or a biopsy. The most common use of flow cytometry is in the identification of markers on cells, particularly in the immune system (called immunophenotyping).
Immunohistochemistry
Immunohistochemistry (IHC) is a special staining process that involves adding a chemical marker to immune cells. The cells are then studied using a microscope. IHC looks for the immunophenotype of cells from a biopsy or tissue sample.

Imaging tests
Imaging tests take pictures of the inside of your body to look for cancer deposits. A radiologist, an expert in interpreting imaging tests, will write a report and send this report to your doctor. Your doctor will discuss the results with you. While these reports are available to you through your portal, please wait to discuss these results with your doctor.

The following imaging tests are listed in alphabetical order and not in order of importance.

CT scan
A computed tomography (CT or CAT) scan uses x-rays and computer technology to take pictures of the inside of the body. It takes many x-rays of the same body part from different angles. All the images are combined to make one detailed picture.

A CT scan of your chest, abdomen, and/or pelvis may be one of the tests to look for cancer. In most cases, contrast will be used.

Contrast
Contrast material is used to improve the pictures of the inside of the body. Contrast materials are not dyes, but substances that help enhance and improve the images of several organs and structures in the body. It is used to make the pictures clearer. The contrast is not permanent and will leave the body in your urine after the test. The types of contrast vary and are different for CT and MRI.

Tell your doctors if you have had allergic reactions to contrast in the past - especially to iodine or shellfish like shrimp. This is important. You might be given medicines to avoid the effects of those allergies. Contrast might not be used if you have a serious allergy or if your kidneys aren’t working well.

MRI scan
A magnetic resonance imaging (MRI) scan uses radio waves and powerful magnets to take pictures of the inside of the body. It does not use x-rays. Tell the technician if you have any metal in your body.

PET scan
A positron emission tomography (PET) scan uses a radioactive drug called a tracer. A tracer is a substance injected into a vein to see where cancer cells are in the body and if they are using sugar produced by your body to grow. Cancer cells show up as bright spots on PET scans because they use sugar more quickly than other cells. However, not all tumors will appear on a PET scan. Also, not all bright spots are cancer. It is normal for the brain, heart, kidneys, and bladder to be bright on PET. When a PET scan is combined with CT, it is called a PET/CT scan. It may be done with one or two machines depending on the cancer center.
Heart tests

Certain treatments can affect heart (cardiac) function. Heart tests might be used to see how well your heart works. These tests might be used as a baseline and before giving chemotherapy. You might be referred to a heart specialist called a cardiologist.

**Electrocardiogram**
An electrocardiogram (ECG or EKG) shows electrical changes in your heart. It reveals information about your heart rate and rhythm. Prolonged corrected QT interval (or QTc) occurs when your heart muscle takes longer than normal to recharge between beats. Often, this electrical disturbance can be seen on an ECG. Certain treatments for MZL can cause prolonged QTc. If the QTc becomes too prolonged, it can cause dangerous heart rhythms.

**Echocardiogram**
An echocardiogram (or echo) uses sound waves to make pictures. For this test, small patches will be placed on your chest to track your heartbeat. Next, a wand with gel on its tip will be slid across part of your bare chest. A picture of your beating heart will be seen on a screen. The pictures will be recorded for future viewing.

An echocardiogram is one way of measuring ejection fraction, which is the amount of blood pumped out of the left side of your heart every time it beats. In low ejection fraction, the amount of blood pumping from the left side of the heart is lower than normal.

**Cardiac nuclear medicine scan**
A nuclear heart scan is an imaging test that uses special cameras and a radioactive substance called a tracer to create pictures of your heart. The tracer is injected into your blood and travels to your heart. This test can also be used to measure the ejection fraction.

**MUGA**
A multigated acquisition (MUGA) scan is used to evaluate the pumping function of your heart. During the test, a small amount of radiotracer is injected into a vein. A special camera, called a gamma camera, will create computer-generated movie images of your beating heart.

MUGA scan might show low ejection fraction. This is when the amount of blood pumping from the left side of the heart is lower than normal.
Key points

- Blood and imaging tests check for signs of disease, how well organs are working, and treatment results.
- A biopsy is the removal of a sample tissue or fluid for testing. It is an important part of an accurate MZL diagnosis.
- Immunophenotyping is used to distinguish MZL from other types of lymphoma.
- A sample from your biopsy may undergo lab tests to look for specific DNA (deoxyribonucleic acid) mutations/alterations, protein levels, or other molecular features. This information is used to learn more about your subtype of MZL.
- Biomarker testing includes tests of genes or their products (proteins). It identifies the presence or absence of mutations and certain proteins.
- Imaging tests are used to look for areas of lymphoma involvement and are part of your staging workup.
- Certain treatments can affect heart function. Heart tests might be used to see how well your heart works.
- Online patient portals are a great way to access your test results. Be sure to discuss these results with your care team before drawing any conclusions about what the results might mean.

Take our survey
And help make the NCCN Guidelines for Patients better for everyone!

NCCN.org/patients/comments
### 3 Treatment overview

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There is more than one treatment for marginal zone lymphoma. This chapter presents an overview of the possible types of treatment and what to expect. Not everyone will receive the same treatment. Treatment options are based on many factors. Together, you and your care team will choose a treatment plan that is right for you.

Marginal zone lymphoma (MZL) is highly treatable and may be curable in certain circumstances. Treatment for MZL usually consists of radiation therapy, chemotherapy, immunotherapy, targeted therapy, antibiotic therapy, or combinations of these treatments (often called chemoimmunotherapy). Surgery may be an option in very select cases of localized marginal zone lymphoma.

It is important to have regular talks with your care team about your goals for treatment and your treatment plan.

Treatment team

Treating MZL takes a team approach. Treatment decisions should involve a multidisciplinary team (MDT). An MDT is a team of doctors, health care workers, and social care professionals from different professional backgrounds who have knowledge (expertise) and experience with your type of cancer. This team is united in the planning and implementing of your treatment. Ask who will coordinate your care.

Some members of your care team will be with you throughout cancer treatment, while others will only be there for parts of it. Get to know your care team and help them get to know you.

Depending on your diagnosis, your team might include the following:

- **A hematologist or hematologic oncologist** is a medical expert in blood diseases and blood cancers.
- **A pathologist or hematopathologist** analyzes the cells and tissues removed during a biopsy and provides cancer diagnosis, staging, and information about biomarker testing.
- **A diagnostic radiologist** interprets the results of x-rays and other imaging tests.
- **An interventional radiologist** performs needle biopsies and places intravenous (IV) ports for treatment.
- **A medical oncologist** treats cancer in adults using systemic therapy.
- **A gastroenterologist** is an expert in diseases of the digestive tract.
- **A radiation oncologist** prescribes and plans radiation therapy to treat cancer.
- **An anesthesiologist** gives anesthesia, a medicine so you do not feel pain during surgery or procedures.
- **Residents and fellows** are doctors who are continuing their training, some to become specialists in a certain field of medicine.
- **Nurse practitioners and physician assistants** are health care providers. Some of your clinic visits may be done by a nurse practitioner or physician assistant.
Oncology nurses provide your hands-on care, like giving systemic therapy, managing your care, answering questions, and helping you cope with side effects. Sometimes, these experts are called nurse navigators.

Oncology pharmacists provide medicines used to treat cancer and to manage symptoms and side effects.

Palliative care nurses, advanced practice providers, and physicians help provide an extra layer of support with your cancer-related symptoms.

Nutritionists and dietitians can provide guidance on what foods are most suitable for your condition.

An occupational therapist helps people with the tasks of daily living.

A physical therapist helps people move with greater comfort and ease.

A certified lymphedema therapist gives a type of massage called manual lymph drainage.

Psychologists and psychiatrists are mental health experts who can help manage issues such as depression, anxiety, or other mental health conditions that can affect how you feel.

Social workers help people solve and cope with problems in their everyday lives. Clinical social workers also diagnose and treat mental, behavioral, and emotional issues. The anxiety a person feels when diagnosed with cancer might be managed by a social worker in some cancer centers. They, or other designated workers, can help navigate the complexities of financial and insurance stresses.

A research team helps to collect research data and coordinate care if you are in a clinical trial. Clinical trials help bring new therapies to patients and advance the treatment for everyone. Consider asking your care team about access to clinical trials.

Your physical, mental, and emotional well-being are important. You know yourself better than anyone. Help other team members understand:

- How you feel
- What you need
- What is working and what is not

Keep a list of names and contact information for each member of your team. This will make it easier for you and anyone involved in your care to know whom to contact with questions or concerns.

International Prognostic Index

The International Prognostic Index (IPI) is a scoring system for prognosis in those with lymphoma. A prognosis is the likely course your disease will take. IPI is based on age, performance status (PS), cancer stage, lactate dehydrogenase (LDH) results, and if cancer is found in the bone marrow, central nervous system (CNS), liver, gastrointestinal tract, or lung.
Treatment phases

Here are some terms you might hear used by your care team.

**Induction**
Induction or first-line therapy is the first phase of treatment. The goal of induction is complete response (CR) or remission. After induction, you will have tests to look for a response (remission).

**Consolidation**
For those in remission, consolidation may occur after induction. It is used to kill any cancer cells that might be left in the body after induction. This is to prevent cancer from returning. Sometimes, this treatment is called post-remission therapy, which might be a combination of consolidation and maintenance therapy. Not everyone will receive consolidation therapy.

**Maintenance**
Maintenance can be the third phase of treatment. It is treatment to prevent cancer from returning. It may be given for a long time and occur over years. Maintenance is also called post-consolidation therapy because it is treatment after (post) consolidation. Not everyone will receive maintenance therapy. Maintenance may be recommended depending on your type of disease, consolidation, and risk of relapse.

**Remission**
There are different types of treatment responses. When there are no signs of cancer, it is called a complete response (CR) or complete remission. Remission can be short-term (temporary) or long-lasting (permanent).

In partial response, cancer is still present, but it has reduced in size.

**Relapse**
When cancer returns after a period of remission, it is called a relapse. The goal of treatment is to achieve remission again. A relapse is very serious. It is important to ask about your prognosis.

**Refractory**
When cancer has not gone away and does not respond to treatment, it is called refractory or resistant cancer. The cancer may be resistant at the start of treatment or it may become resistant during treatment. Refractory disease is very serious. It is important to ask about your prognosis.

**Surveillance**
You will be monitored throughout treatment. Surveillance watches for any changes in your condition after remission or a hematopoietic cell transplant. You will have tests during surveillance to check for relapse.

**Observation without treatment**
Some slow-growing (indolent) lymphomas do not require immediate treatment, including MZL. Observation is sometimes called active surveillance or “watch and wait.” During observation, your care team will monitor for symptoms to appear. Once specific signs or symptoms appear, you will start treatment. Ask your care team what specific signs or symptoms they will be looking for.
Preventing pregnancy during treatment

If you become pregnant during chemotherapy, radiation therapy, or other types of systemic therapy, serious birth defects can occur. Speak with your care team about preventing pregnancy while being treated for cancer. Those who want to become pregnant in the future should be referred to a fertility specialist to discuss the options before starting chemotherapy and/or radiation therapy.

Systemic therapy

Systemic therapy is drug therapy that works throughout the body. Types include chemotherapy, targeted therapy, and immunotherapy. Systemic therapy might be used alone or with other therapies. Goals of systemic therapy should be discussed before starting treatment. The choice of therapy takes into consideration many factors, including age, other serious health issues, and future treatment possibilities like a stem cell transplant. Your preferences about treatment are important. If you have any religious or personal beliefs about certain kinds of treatment, now would be the time to share them with your care team.

Warnings!

You might be asked to stop taking or avoid certain food or herbal supplements when on a systemic therapy. Some supplements and food can affect the ability of a drug to do its job. This is called a drug interaction. It is critical to speak with your care team about any supplements you may be taking.

Some examples include:

- Turmeric
- Gingko biloba
- Green tea extract
- St. John’s Wort

Certain medicines can also affect the ability of a drug to do its job. Antacids, heart medicine, and antidepressants are just some of the medicines that might interact with a systemic therapy. This is why it is important to tell your doctor about any medications, vitamins, over-the-counter (OTC) drugs, herbals, or supplements you are taking. Bring a list with you to every visit.
First-line therapy
First-line systemic therapy is the first drug treatment given. For a list of first-line therapy options, see Guide 1.

### Did you know?

The terms “chemotherapy” and “systemic therapy” are often used interchangeably, but they are not the same. Chemotherapy, targeted therapy, and immunotherapy are all types of systemic therapy.

### Guide 1

**First-line therapy options**

<table>
<thead>
<tr>
<th>Preferred options</th>
<th>Other options</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Bendamustine with rituximab</td>
<td>• Lenalidomide with rituximab</td>
</tr>
<tr>
<td>• Cyclophosphamide, doxorubicin, vincristine, and prednisone with rituximab (RCHOP)</td>
<td>• Rituximab for extranodal MZL and nodal MZL</td>
</tr>
<tr>
<td>• Cyclophosphamide, vincristine, and prednisone (CVP) with rituximab</td>
<td>For those who are older or unwell:</td>
</tr>
<tr>
<td>• Rituximab for those with splenic MZL or those who are older or unwell</td>
<td>• Chlorambucil with or without rituximab</td>
</tr>
<tr>
<td></td>
<td>• Cyclophosphamide with or without rituximab</td>
</tr>
</tbody>
</table>

*Note: An FDA-approved biosimilar might be used for rituximab.
## Second-line therapy
Second-line therapy is the next set of treatment given if cancer progresses during or after systemic therapy. After 3 or more lines of systemic therapy, CAR T-cell therapy (axicabtagene ciloleucel) might be given. See Guide 2.

### Guide 2
Second-line and next-line therapy options

<table>
<thead>
<tr>
<th>Preferred options</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Bendamustine with obinutuzumab or rituximab (not recommended if you had bendamustine before)</td>
</tr>
<tr>
<td>• Ibrutinib</td>
</tr>
<tr>
<td>• Zanubrutinib</td>
</tr>
<tr>
<td>• Cyclophosphamide, doxorubicin, vincristine, and prednisone with rituximab (RCHOP)</td>
</tr>
<tr>
<td>• Cyclophosphamide, vincristine, and prednisone (CVP) with rituximab</td>
</tr>
<tr>
<td>• Lenalidomide with rituximab</td>
</tr>
<tr>
<td>• Rituximab</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Other recommended</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Copanlisib for relapsed/refractory disease after two prior therapies</td>
</tr>
<tr>
<td>• Rituximab</td>
</tr>
<tr>
<td>• Ibritumomab tiuxetan</td>
</tr>
<tr>
<td>• Cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP) with obinutuzumab</td>
</tr>
<tr>
<td>• CVP with obinutuzumab</td>
</tr>
<tr>
<td>• Lenalidomide with obinutuzumab</td>
</tr>
</tbody>
</table>

For those who are older or unwell:
- Chlorambucil with or without rituximab
- Cyclophosphamide with or without rituximab

*Note: An FDA-approved biosimilar might be used for rituximab.*
Chemotherapy

Chemotherapy kills fast-dividing cells throughout the body, including cancer cells and some normal cells. More than one chemotherapy may be used to treat MZL. When only one drug is used, it’s called a single agent. A combination or multi-agent regimen is the use of two or more chemotherapy drugs.

Some chemotherapy drugs are liquids that are infused into a vein or injected under the skin with a needle. Other chemotherapy drugs may be given as a pill that is swallowed. The final dose differs between people because it is based on body weight and height. Intrathecal chemotherapy is injected into spinal or brain fluid.

In most cases, chemotherapy is given in cycles of treatment days followed by days of rest. This allows the body to recover before the next cycle. Cycles vary in length depending on which chemotherapy is used. You will have tests to see how well treatment is working. You might spend time in the hospital during treatment.

Examples of chemotherapy drugs include:

- Bendamustine (Treanda, Bendeka)
- Chlorambucil (Leukeran)
- Cyclophosphamide (Cytoxan, Neosar)
- Doxorubicin (Adriamycin, Rubex)
- Vincristine (Oncovin, Vincasar Pfs)

This is an example of a chemotherapy drug combination (regimen):

- CVP is cyclophosphamide, vincristine, and prednisone.

Chemoimmunotherapy

Chemoimmunotherapy, also called immunochemotherapy, includes chemotherapy and immunotherapy drugs to treat cancer.

One example:

- RCHOP is rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone.
Immunotherapy

Immunotherapy is drug therapy that increases the activity of your immune system. By doing so, it improves your body’s ability to find and destroy cancer cells. Immunotherapy can be given alone or with other types of treatment. Lenalidomide (Revlimid) is an example of an immunotherapy modulator.

Monoclonal antibody therapy

Antibody therapy uses antibodies to help the body fight cancer, infection, or other diseases. Antibodies are proteins made by the immune system that bind to specific markers on cells or tissues. Monoclonal antibodies (mAbs) used in cancer treatment may kill cancer cells directly, block development of tumor blood vessels, or help the immune system kill cancer cells. As with other treatments, there is the potential for complications.

- Rituximab (Rituxan) works against the protein CD20 found on the surface of B cells. When it binds to this protein it triggers cell death. A biosimilar or substitute might be used in place of rituximab. A biosimilar is almost an identical drug made by another company. It must be used in the exact same way and at the same dose as rituximab. Biosimilars include: Riabni, Hycela, Ruxience, and Truxima.
- Other mAb therapy examples include obinutuzumab (Gazyva) and ibritumomab tiuxetan (Zevalin).

CD19-targeting CAR T-cell therapy

CD19-directed genetically modified autologous T-cell immunotherapy (CD19-targeting CAR T-cell therapy) or anti-CD19 CAR T-cell therapy is made from your own T cells. T cells will be removed from your body, and in the lab, a CAR (chimeric antigen receptor) will be added to them. This programs the T cells to find the cancer cells. The programmed T cells will be infused back into your body to find and kill cancer cells. This treatment is not for everyone. There can be severe and sometimes life-threatening reactions.

There are currently 4 CAR T-cell therapies FDA-approved in different subtypes of lymphoma. While none is specifically FDA-approved for marginal zone lymphomas, axicabtagene ciloleucel (Yescarta) has been studied in this disease and is a recommended option in the third-line or later treatment.

More information on CAR T-cell therapy can be found in *NCCN Guidelines for Patients: Immunotherapy Side Effects*, available at NCCN.org/patientguidelines.
Targeted therapy

Targeted therapy is drug therapy that focuses on specific or unique features of cancer cells. Targeted therapies seek out how cancer cells grow, divide, and move in the body. These drugs stop the action of molecules that help cancer cells grow and/or survive. Acalabrutinib (Calquence), ibrutinib (Imbruvica), and zanubrutinib (Brukinsa) are examples of a type of targeted therapy called Bruton tyrosine kinase inhibitors (BTKi). These drugs block the activity of BTK that leads to growth of B cells.

Radiation therapy

Radiation therapy (RT) uses high-energy radiation from photons, electrons, or protons, and other sources to kill cancer cells and shrink tumors. It is given over a certain period of time. Radiation therapy can be given alone or with certain systemic therapies. When used as supportive care to help ease pain or discomfort caused by cancer, it is called palliative RT.

A four-dimensional (4D) CT scan might be used to plan RT. A 4D-CT records multiple images over time. It allows playback of the scan as a video, so that internal movement can be tracked and observed.

EBRT

External beam radiation therapy (EBRT) uses a machine outside of the body to aim radiation at the tumor(s) or areas of the body.

Common types of EBRT that may be used to treat your cancer include the following:

- **Three-dimensional conformal radiation therapy (3D-CRT)** uses computer software and CT images to aim beams that match the shape of the tumor.
- **Intensity-modulated radiation therapy (IMRT)** uses small beams of different strengths to match the shape of the tumor.
- **Involved-site radiation therapy (ISRT)** treats cancer found in or near lymph nodes (nodal disease)

**Total body irradiation**

Total body irradiation (TBI) is radiation of the whole body given before bone marrow transplant.
Hematopoietic cell transplant

A hematopoietic cell transplant (HCT) replaces hematopoietic stem cells that have been destroyed by high doses of chemotherapy and/or radiation therapy as part of the transplant process. A hematopoietic stem cell is an immature cell that can develop into any type of blood cell. You might hear it called a stem cell transplant (SCT) or a bone marrow transplant (BMT). This book will refer to it as HCT. HCTs are performed in specialized centers.

There are 2 types of HCTs:

- **Autologous** – stem cells come from you
- **Allogeneic** – stem cells come from a donor who may or may not be related to you

Autologous transplant

An autologous transplant is also called HDT/ASCR (high-dose therapy with autologous stem cell rescue) or an autoHCT. First, your healthy stem cells will be removed. Then, you will receive highly intensified treatment to kill remaining lymphoma cells and your normal bone marrow cells will be killed as well. Your healthy stem cells will be returned to “rescue” your marrow and allow regrowth of your blood and immune system.

Allogeneic transplant

An allogeneic transplant uses healthy stem cells from a donor. The donor may or may not be related to you. An allogeneic HCT (alloHCT) is sometimes used to treat a relapse.

Before an HCT, treatment is needed to destroy bone marrow cells. This is called conditioning and it creates room for the healthy donor stem cells. It also weakens the immune system so your body will accept and won’t kill the transplanted cells. Chemotherapy is used for conditioning. Radiation therapy may also be given as part of conditioning treatment.

After conditioning, you will receive a transfusion of the healthy stem cells from a donor that has been matched to you. A transfusion is a slow injection of blood products into a vein. This can take several hours. The transplanted stem cells will travel to your bone marrow and grow. New, healthy blood cells will form. This is called engraftment. It usually takes about 2 to 4 weeks. Until then, you will have little or no immune defense. You may need to stay in a very clean room at the hospital or be given antibiotics to prevent or treat infection. Transfusions are also possible. A red blood cell transfusion is used to prevent bleeding and to treat anemia (below normal red blood cell count). A platelet transfusion is used to treat a low platelet count or bleeding. While waiting for the cells to engraft, you will likely feel tired and weak.

**Possible side effects**

Every treatment has side effects. You will be monitored for infections, disease relapse, and graft-versus-host disease (GVHD). In GVHD, the donor cells attack your normal, healthy tissue. There are treatments for GVHD. Ask your doctor about the possible side effects or complications of HCT and how this might affect your quality of life.

More information on GVHD can be found in *NCCN Guidelines for Patients: Graft-Versus-Host Disease*, available at [NCCN.org/patientguidelines](https://www.nccn.org/).
Surgery

Surgery is an operation or procedure to remove cancer from the body. Surgery might include the removal of the spleen called a splenectomy. If surgery is needed, seek the opinion of an experienced surgeon. The surgeon should be an expert in performing your type of surgery in those with MZL. Hospitals that perform many surgeries often have better results. You can ask for a referral to a hospital or cancer center that has experience in treating your type of cancer.

Clinical trials

A clinical trial is a type of medical research study. After being developed and tested in a laboratory, potential new ways of fighting cancer need to be studied in people. If found to be safe and effective in a clinical trial, a drug, device, or treatment approach may be approved by the U.S. Food and Drug Administration (FDA). All drugs that are currently available are because of previous clinical trials.

Everyone with cancer should carefully consider all of the treatment options available for their cancer type, including standard treatments and clinical trials. Talk to your doctor about whether a clinical trial may make sense for you.

Phases

Most cancer clinical trials focus on treatment. Treatment trials are done in phases.

- **Phase I trials** study the dose, safety, and side effects of an investigational (new) drug or treatment approach. They also look for early signs that the drug or approach is helpful.
- **Phase II trials** study how well the drug or approach works against a specific type of cancer.
- **Phase III trials** test the drug or approach against a standard treatment. If the results are good, it may be approved by the FDA.
- **Phase IV trials** study the long-term safety and benefit of an FDA-approved treatment.

Who can enroll?

Every clinical trial has rules for joining, called eligibility criteria. The rules may be about age, cancer type and stage, treatment history, or general health. These requirements ensure that participants are alike in specific ways and that the trial is as safe as possible for the participants.

Informed consent

Clinical trials are managed by a group of experts called a research team. The research team will review the study with you in detail, including its purpose and the risks and benefits of joining. All of this information is also provided in an informed consent form. Read the form carefully and ask questions before signing it. Take time to discuss with family, friends, or others whom you trust. Keep in mind that you can leave and seek treatment outside of the clinical trial at any time.
Start the conversation
Don’t wait for your doctor to bring up clinical trials. Start the conversation and learn about all of your treatment options. If you find a study that you may be eligible for, ask your treatment team if you meet the requirements. If you have already started standard treatment you may not be eligible for certain clinical trials. Try not to be discouraged if you cannot join. New clinical trials are always becoming available. Clinical trials are not just for those who have few remaining treatment options. They can be considered at almost any stage of treatment.

Frequently asked questions
There are many myths and misconceptions surrounding clinical trials. The possible benefits and risks are not well understood by many with cancer.

Will I get a placebo?
Placebos (inactive versions of real medicines) are almost never used alone in cancer clinical trials. It is common to receive either a placebo with a standard treatment, or a new drug with a standard treatment. You will be informed, verbally and in writing, if a placebo is part of a clinical trial before you enroll.

Are clinical trials free?
There is no fee to enroll in a clinical trial. The study sponsor pays for research-related costs, including the study drug. You may, however, have costs indirectly related to the trial, such as the cost of transportation or child care due to extra appointments. During the trial, you will continue to receive standard cancer care. This care is billed to—and often covered by—insurance. You are responsible for copays and any costs for this care that are not covered by your insurance.

Finding a clinical trial

In the United States
NCCN Cancer Centers
NCCN.org/cancercenters

The National Cancer Institute (NCI)
cancer.gov/about-cancer/treatment/clinical-trials/search

Worldwide
The U.S. National Library of Medicine (NLM)
clinicaltrials.gov

Need help finding a clinical trial?
NCI’s Cancer Information Service (CIS)
1.800.4.CANCER (1.800.422.6237)
cancer.gov/contact
Supportive care

Supportive care is health care given during all cancer stages. It aims to prevent, reduce, and relieve suffering, and to improve quality of life. Supportive care might include pain relief (palliative care), emotional or spiritual support, financial aid, or family counseling. Tell your care team how you are feeling and about any side effects so they can be managed. Best supportive care, supportive care, and palliative care are often used interchangeably.

It is very important to take care of yourself by eating well, drinking plenty of fluids, exercising, and doing things that make you feel energized. Strength is needed to sustain you during treatment.

Some potential side effects and procedures are described next. They are not listed in order of importance. Some side effects are very rare.

Anemia, neutropenia, and thrombocytopenia

Some cancer treatments can cause low blood cell counts.

- **Anemia** is a condition where your body does not make enough healthy blood cells, resulting in less oxygen being carried to your cells. You might tire easily if you are anemic.

- **Neutropenia** is a decrease in neutrophils, the most common type of white blood cell. This puts you at risk for infection.

- **Thrombocytopenia** is a condition where there are not enough platelets found in the blood. This puts you at risk for bleeding.

For more information on anemia, neutropenia, and thrombocytopenia, see *NCCN Guidelines for Patients: Anemia and Neutropenia*, available at [NCCN.org/patientguidelines](http://NCCN.org/patientguidelines).

Distress

Depression, anxiety, and sleeping problems are common and a normal part of a cancer diagnosis. Talk to your doctor and with those whom you feel most comfortable about how you are feeling. There are services, people, and medicine that can help you. Support and counseling services are available.

For more information, see *NCCN Guidelines for Patients: Distress During Cancer Care*, available at [NCCN.org/patientguidelines](http://NCCN.org/patientguidelines).

Fatigue

Fatigue is extreme tiredness and inability to function due to lack of energy. Fatigue may be caused by cancer or it may be a side effect of treatment. Let your care team know how you are feeling and if fatigue is getting in the way of doing the things you enjoy. Eating a balanced diet, exercise, yoga, and massage therapy can help. You might be referred to a nutritionist or dietitian to help with fatigue.
Hair loss
Chemotherapy may cause hair loss (alopecia) all over your body—not just on your scalp. Some chemotherapy drugs are more likely than others to cause hair loss. Dosage might also affect the amount of hair loss. Most of the time, hair loss from chemotherapy is temporary. Hair often regrows 3 to 6 months after treatment ends. Your hair may be a different shade or texture.

Scalp cooling
Scalp cooling (or scalp hypothermia) might help lessen hair loss in those receiving certain types of chemotherapy. Some people find scalp cooling uncomfortable and have headaches as a side effect from the cold. You may experience hair loss even with scalp cooling treatment.

Hypersensitivity, allergy, and anaphylaxis
Certain treatments can cause an unwanted reaction. Hypersensitivity is an exaggerated response by the immune system to a drug or other substance. This can include hives, skin welts, and trouble breathing. An allergy is an immune reaction to a substance that normally is harmless or would not cause an immune response in most people. An allergic response may cause harmful symptoms such as itching or inflammation (swelling). Anaphylaxis or anaphylactic shock is a severe and possible life-threatening allergic reaction.

Infections
Infections can be caused by viruses, fungus, or bacteria. Antibiotics can treat bacterial infections. Antifungal medicines can treat fungal infections. You may be given antiviral drugs to prevent viral infections.

Late effects
Late effects are side effects that occur months or years after a disease is diagnosed or after treatment has ended. Late effects may be caused by cancer or cancer treatment. They may include physical, mental, and social problems, and second cancers. The sooner late effects are treated the better. Ask your care team about what late effects could occur. This will help you know what to look for.

Lymphedema
Lymphedema is a condition in which extra lymph fluid builds up in tissues and causes swelling. It may be caused when part of the lymph system is damaged or blocked, such as during surgery to remove lymph nodes, or by radiation therapy. Cancers that block lymph vessels can also cause lymphedema. Swelling usually develops slowly over time. It may develop during treatment or it may start years after treatment. If you have lymphedema, you may be referred to an expert in lymphedema management. The swelling may be reduced by exercise, massage, compression sleeves, and other means. Ask your care team about the ways to treat lymphedema.

Nausea and vomiting
Nausea and vomiting are a common side effect of treatment. You will be given medicine to prevent and treat nausea and vomiting.
Treatment overview

Supportive care

For more information, see NCCN Guidelines for Patients: Nausea and Vomiting, available at NCCN.org/patientguidelines.

**Neurocognitive effects**
Some treatments can damage the nervous system (neurotoxicity) causing problems with concentration and memory. Survivors are at risk for neurotoxicity and might be recommended for neuropsychological testing. Neuropsychology looks at how the health of your brain affects your thinking and behavior. Neuropsychological testing can identify your limits and doctors can create a plan to help with these limits.

**Neuropathy**
Neuropathy is a nerve problem that causes pain, numbness, tingling, swelling, or muscle weakness in different parts of the body. It usually begins in the hands or feet and gets worse over time. Neuropathy may be caused by cancer or cancer treatment such as chemotherapy.

**Pain**
Tell your care team about any pain or discomfort. You might meet with a palliative care specialist or with a pain specialist to manage pain.

**Side effects**
All cancer treatments can cause unwanted health issues called side effects. Side effects depend on many factors. These factors include the drug type and dose, length of treatment, and the person. Some side effects may be harmful to your health. Others may just be unpleasant. Cancer treatment can cause a number of side effects. Some are very serious.

---

**Keep a pain diary**
A pain diary is a written record that helps you keep track of when you have pain, how bad it is, what causes it, and what makes it better or worse. Use a pain diary to discuss your pain with your care team. You might be referred to a specialist for pain management.

Include in your pain diary:
- The time and dose of all medicines
- When pain starts and ends or lessens
- Where you feel pain
- Describe your pain. Is it throbbing, sharp, tingling, shooting, or burning? Is it constant, or does it come and go?
- Does the pain change at different times of day? When?
- Does the pain get worse before or after meals? Does certain food or drink make it better?
- Does the pain get better or worse with activity? What kind of activity?
- Does the pain keep you from falling asleep at night? Does pain wake you up in the night?
- Rate your pain from 0 (no pain) to 10 (worst pain you have ever felt)
- Does pain get in the way of you doing the things you enjoy?
Ask for a complete list of side effects of your treatments. Also, tell your treatment team about any new or worsening symptoms. There may be ways to help you feel better. There are also ways to prevent some side effects.

**Therapy-related toxicity**
Many of the drug therapies used to treat marginal zone lymphoma can be harmful to the body. You will be closely monitored for therapy-related toxicity.

**Trouble eating**
Sometimes side effects from surgery, cancer, or other treatments might cause you to feel not hungry or sick to your stomach (nauseated). You might have a sore mouth. Healthy eating is important during treatment. It includes eating a balanced diet, eating the right amount of food, and drinking enough fluids. A registered dietitian who is an expert in nutrition and food can help. Speak to your care team if you have trouble eating or maintaining your weight.

**Tumor lysis syndrome**
Cancer treatment causes cell death. In tumor lysis syndrome (TLS), waste released by dead cells builds up in the body causing kidney damage and severe blood electrolyte disturbances. Changes in creatinine, lactic acid, uric acid, phosphorus (Phos), potassium (K), and calcium (Ca) levels can be a sign of TLS. TLS can be life-threatening.

**Survivorship**
After treatment, your health will be monitored for side effects of treatment and the return of cancer. This is part of your survivorship care plan. It is important to keep any follow-up doctor visits and imaging test appointments. Seek good routine medical care, including regular doctor visits for preventive care and cancer screening.

You should discuss a personalized survivorship care plan with your care team. It will contain a summary of possible long-term effects of treatment called late effects and list follow-up tests. Find out how your primary care provider will coordinate with specialists for your follow-up care.

For more information on survivorship, see NCCN.org/patientguidelines.
Key points

- Treatment decisions should involve a multidisciplinary team (MDT) from different fields of medicine who have knowledge (expertise) and experience with your type of cancer.

- Marginal zone lymphoma (MZL) is highly treatable and curable in certain circumstances. The goal of treatment is to achieve a complete response (CR) or remission.

- Systemic therapy works throughout the body. It includes chemotherapy, targeted therapy, and immunotherapy.

- Radiation therapy (RT) uses high-energy radiation from photons, protons, electrons, and other sources to kill cancer cells and shrink tumors.

- Chemotherapy kills fast-dividing cells throughout the body, including cancer cells and some normal cells.

- Immunotherapy is drug therapy that increases the activity of your immune system.

- Targeted therapies can block the ways cancer cells grow, divide, and move in the body.

- Treatment can affect fertility in all sexes. Those who want to have children in the future should be referred to a fertility specialist before starting chemotherapy and/or radiation therapy to discuss the options.

- A hematopoietic cell transplant (HCT) replaces damaged bone marrow stem cells with healthy stem cells. You might hear it called a stem cell transplant (SCT) or bone marrow transplant (BMT).

- Clinical trials study how safe and helpful tests and cancer treatments are for people.

- Supportive care is health care that relieves symptoms caused by cancer or its treatment and improves quality of life. Supportive care is always given.

- All cancer treatments can cause unwanted health issues called side effects. It is important for you to tell your care team about all your side effects so they can be managed.

- Eating a balanced diet, drinking enough fluids, exercise, yoga, and massage therapy can help manage side effects.

- Some side effects, called late effects, may take years to appear. Risk for late effects will depend on the type(s) of cancer treatment you had, and the dose and the length of time you were treated. It is important to keep follow-up appointments.
Extranodal MZL (stomach only)

- Overview
- Testing
- Treatment
- Stage 1
- Stages 2, 2E, and 4
- Recurrence
- Key points
Extranodal marginal zone lymphoma (ENMZL) can be found in almost every part of the body with the stomach being the most common site. This chapter is for ENMZL (gastric). Together, you and your care team will choose a treatment plan that is right for you.

Overview

Extranodal marginal zone lymphoma (ENMZL) can be found in almost every part of the body. However, the stomach is the most common site. This type of marginal zone lymphoma forms in cells in the mucosa that help make antibodies. The mucosa is the innermost layer of wall of the digestive tract. Those with ENMZL (gastric) may also have Helicobacter gastritis or an autoimmune disease, such as Hashimoto thyroiditis or Sjögren syndrome.

Most ENMZLs are low-grade lesions that grow slowly and do not tend to spread to other places in the body.

The digestive tract

The digestive system takes in and breaks down food, absorbs nutrients, and removes waste from the body. The digestive or gastrointestinal (GI) tract is part of the digestive system. It includes the esophagus, stomach, small intestine, colon, and rectum. The innermost layer of the GI tract is called the mucosa.

The digestive tract

The digestive or gastrointestinal (GI) tract is part of the digestive system. Food enters the mouth and passes through the esophagus into the stomach. After being broken down into a liquid, food enters the small intestine. The large intestine prepares unused food to be moved out of the body.
Stages
A cancer stage is a way to describe the extent of the cancer at the time you are first diagnosed. The American Joint Committee on Cancer (AJCC) created a staging system to determine how much cancer is in your body, where it is located, and what subtype you have. AJCC is just one type of staging system.

Staging is based on a combination of information to reach a final numbered stage. Often, not all information is available at the initial evaluation. More information can be gathered as treatment begins. Doctors may explain your cancer stage in different ways than described next.

- In early-stage or stage 1 disease, cancer is confined to the stomach.
- In stage 2 disease, cancer is found in the lymph nodes.
- In stage 2E disease, cancer has grown through the layers of the stomach wall and into nearby organs and tissues.
- In stage 4 disease, cancer is found on both sides of the diaphragm or in distant sites (metastases) such as bone marrow or distant lymph nodes.

Layers of the stomach wall
The wall of the stomach is made up of 5 layers: mucosa, submucosa, muscle layer, subserosa, and serosa.
Lymph nodes
ENMZL (gastric) can sometimes spread from the stomach to lymph nodes. There are hundreds of lymph nodes throughout your body. They work as filters to help fight infection and remove harmful things from your body. Regional lymph nodes are found near the stomach.

Lymph drains from the stomach wall into lymphatic vessels in the mucosa and submucosa. From here it drains into lymph nodes outside the stomach. Regional lymph nodes include pyloric (pylorus area of stomach), perigastric, pericardiac at the esophagogastric junction, and lymph nodes near organs and arteries such as the pancreas, spleen (splenic), and liver (hepatic).

The largest group of stomach lymph nodes are the perigastric lymph nodes found along the lesser and greater curves of the stomach and in the omenta. The omentum is a fold of the thin tissue that lines the abdomen (peritoneum) that surrounds the stomach and other organs in the abdomen.
Testing

ENMZL (gastric) immunophenotype is usually CD10-, CD5-, CD20+, cyclin D1-, and BCL2-.

t(11;18) occurs specifically in some cases of ENMZL (gastric) and is the most frequent genetic abnormality found in this tumor. Translocation is a switching of parts between two chromosomes. A translocation between chromosome 11 and 18 is written as t(11;18). If this translocation is found, the tumor tends not to respond to antibiotic treatment. Therefore, radiation therapy or rituximab will be given with antibiotics.

Tests used to diagnose ENMZL (gastric) are found in Guide 3.

Guide 3
Tests to diagnose gastric MALT

Needed

- Endoscopic biopsy
- IHC panel: CD20, CD3, CD5, CD10, BCL2, kappa/lambda, CD21 or CD23, cyclin D1, and BLC6 with or without cell surface marker analysis by flow cytometry: kappa/lambda, CD19, CD20, CD5, CD23, and CD10
- If positive for H. pylori, then PCR or FISH for t(11;18)

In some cases

- Biomarker testing to detect: immunoglobulin gene rearrangements and MYD88 mutation status to differentiate between Waldenström macroglobulinemia (WM) and marginal zone lymphoma
- Karyotype or FISH: t(1;14); t(3;14); t(11;14); t(11;18)
- FISH or PCR: t(14;18)

H. pylori

Helicobacter pylori or H. pylori is a type of bacterium that causes inflammation and ulcers in the stomach or small intestine. People with H. pylori infections may be more likely to develop cancer in the stomach, including ENMZL (gastric). You will be tested for H. pylori before starting treatment.
### Treatment

Tests used to plan treatment are found in Guide 4.

Any area of diffuse large-B cell lymphoma (DLBCL) should be treated as DLBCL.

For more information on DLBCL, read the *NCCN Guidelines for Patients: Diffuse Large B-Cell Lymphomas*, available at [NCCN.org/patientguidelines](http://NCCN.org/patientguidelines).

### Guide 4

#### Tests to plan treatment

- **Endoscopic biopsy, histology grading, and pathology review**
- **Immunophenotyping with immunohistochemistry (IHC) and flow cytometry**
- **Physical exam with performance status (PS)**
- **Complete blood count (CBC) with differential, lactate dehydrogenase (LDH), comprehensive metabolic panel (CMP), hepatitis B and C testing, and *H. pylori* testing**
- **CT with contrast of chest, abdomen, and pelvis (C/A/T)**
- **Pregnancy test if chemotherapy or radiation therapy willl be used**

**Possible:**
- Bone marrow biopsy with or without aspirate
- PET/CT scan
- Echocardiogram or MUGA scan
- Endoscopy with ultrasound (if available) with multiple biopsies of sites
- Discussion of fertility issues and sperm banking
- SPEP blood test
Stage 1

Since ENMZL (gastric) is often the result of an infection with *H. pylori*, the initial treatment is antibiotic therapy, usually combined with proton pump inhibitors (PPIs). PPIs reduce the production of stomach acid to help prevent or heal ulcers. Many of these lymphomas go away following antibiotic and PPI treatment, although this may take several months. Additional treatment might include radiation therapy or rituximab. Involved-site radiation therapy (ISRT) treats cancer found in or near lymph nodes (nodal disease).

**After treatment with antibiotics only**

After 3 months of treatment, the lymphoma will be restaged with an endoscopic biopsy to see if *H. pylori* or lymphoma remain and to rule out diffuse large B-cell lymphoma (DLBCL).

Treatment options after antibiotics:

- If *H. pylori* remains, then you will be given another round of antibiotics.
- If lymphoma remains and you have symptoms, then you might be given ISRT.
- If both remain and disease is stable, then you will likely be given another round of antibiotics.
- If both remain and disease is progressing or you have symptoms, then you will likely be given antibiotics with ISRT.

**After treatment with ISRT or rituximab**

After 3 to 6 months of treatment, the lymphoma will be restaged with an endoscopic biopsy to see if *H. pylori* or lymphoma remain and to rule out diffuse large B-cell lymphoma (DLBCL).

Treatment options after ISRT or rituximab:

- If *H. pylori* remains, then you might be given another round of antibiotics.
- If lymphoma remains, then you will be given first-line systemic therapy. First-line therapy is the first set of drug treatment given. See Guide 1.
- If both lymphoma and *H. pylori* remain, then you will be given first-line systemic therapy. See Guide 1.
- Continuous active surveillance will be required in all cases even if there is no sign of *H. pylori*.

**Stages 2, 2E, and 4**

Disease that has grown outside the stomach, spread to distant areas of the body, or is causing symptoms might be referred to as distant nodal or advanced stage.

Treatment will likely start when you have any of the following:

- Symptoms
- GI bleeding
- Threatened end-organ function
- Significant bulky disease
- Steady or rapid progression

Treatment includes first-line systemic therapy or ISRT. A clinical trial is always an option even in those without signs or symptoms. First-line therapy options can be found on page 31.
Recurrence

If lymphoma returns after treatment (recurrence) or does not respond to treatment (refractory), treatment options include antibiotics, radiation therapy, second-line systemic therapy, and/or a clinical trial. Second-line therapy is the next set of treatment given if cancer progresses during or after systemic therapy. Sometimes, a hematopoietic cell transplant (HCT) is an option after second-line therapy. After 3 or more lines of systemic therapy, CAR T-cell therapy (axicabtagene ciloleucel) might be given.

Second-line therapy options can be found in Guide 2.

Tell your care team about all side effects so they can be managed.

Key points

- The digestive or gastrointestinal (GI) tract includes the esophagus, stomach, small intestine, colon, and rectum.
- The stomach is the most common site for extranodal marginal zone lymphoma (ENMZL).
- ENMZL (gastric) forms in cells in the innermost layer of the digestive tract called the mucosa.
- ENMZL (gastric) is often the result of an infection with *H. pylori*. Therefore, the initial treatment is antibiotic therapy. Involved-site radiation therapy (ISRT) or rituximab might be added.
- For disease that has grown outside the stomach, spread to distant areas of the body, or is causing symptoms, treatment might include systemic therapy.
- Active surveillance is required in all cases.
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Extranodal MZL (other sites)

53 Overview
53 Testing
54 Treatment
54 Recurrence
56 Key points
Extranodal marginal zone lymphoma (ENMZL) can develop in almost every part of the body. This chapter is for ENMZL not found in the stomach. Together, you and your care team will choose a treatment plan that is right for you.

Overview

Extranodal marginal zone lymphoma (ENMZL) can be found in almost every part of the body. Typical sites include the following: bowel (small and large), breast, head and neck, lung, around the eye (ocular adnexa), ovary, parotid, prostate, and salivary gland. ENMZL may return many years after treatment.

ENMZL of the skin (cutaneous) is not covered in this chapter. For primary cutaneous marginal zone lymphoma (PCMZL), read the NCCN Guidelines for Patients: Primary Cutaneous Lymphomas at NCCN.org/patientguidelines.

Testing

ENMZL immunophenotype is usually CD10-, CD5-, CD20+, CD23/-+, CD43/-+, cyclin D1-, and BCL2-.

t(11;18) occurs specifically in ENMZL and is the most frequent genetic abnormality found in this tumor. Translocation is a switching of parts between two chromosomes. A translocation between chromosome 11 and 18 is written as t(11;18).

Tests used to diagnose non-gastric ENMZL are found in Guide 5.
Extranodal MZL (other sites) Treatment

Treatment
ENMZL can appear in a variety of areas throughout the body. Therefore, treatment is based on the exact location and extent of spread. In cases where primary site is thought to be in the head, neck, or lungs, upper GI endoscopy should be considered.

Tests used to plan treatment are found in Guide 6.

Stage 1 and 2 (limited)
The preferred treatment for disease that is limited to the organ is involved-site radiation therapy (ISRT). When necessary, surgery might be an option for certain sites such as the skin, lung, breast (lumpectomy), thyroid, colon, and small bowel. ISRT might follow surgery. In some cases, rituximab or observation might be options.

Stage 4 (advanced)
Advanced disease has spread to distant sites. Advanced disease is treated with ISRT or systemic therapy. A clinical trial can be considered at any stage.

Follow-up care
After treatment, you be monitored for relapse and disease progression. During this time, you will have a physical exam with lab and imaging tests every 3 to 6 months for 5 years and then every year afterward.

Recurrence

Local
A local recurrence is the return of cancer near the same place as before. You will receive involved-site radiation therapy (ISRT) if you did not receive it before. It will be treated as advanced nodal marginal zone lymphoma (NMZL) as found on page 60.

Systemic
In systemic recurrence, cancer is found in the blood, bone marrow, or in multiple different sites. Treatment will likely start when you have any of the following:

- Symptoms
- GI bleeding
- Threatened end-organ function
- Significant bulky disease
- Steady or rapid progression

If you did not have systemic therapy before, then you will be treated with first-line therapy (see page 31, Guide 1).

If you were previously treated with rituximab, then you will be treated with second-line therapy (see page 32, Guide 2).
## Guide 5
### Tests to diagnose extranodal marginal zone lymphoma (ENMZL)

**Needed**  
- IHC panel: CD20, CD3, CD5, CD10, BCL2, kappa/lambda, CD21 or CD23, and cyclin D1 with or without cell surface marker analysis by flow cytometry: kappa/lambda, CD19, CD20, CD5, CD23, and CD10

**In some cases**  
- Biomarker testing to detect: immunoglobulin gene rearrangements and MYD88 mutation status to differentiate between Waldenström macroglobulinemia (WM) and marginal zone lymphoma, and PCR for t(11;18)
- Karyotype or FISH: t(11;18), t(11;14), t(3;14)
- FISH or PCR: t(14;18)

## Guide 6
### Tests to plan treatment

- Biopsy, histology grading, and pathology review
- Immunophenotyping with immunohistochemistry (IHC) and flow cytometry
- Physical exam with attention to non-gastric sites
- Performance status (PS)
- Complete blood count (CBC) with differential, lactate dehydrogenase (LDH), comprehensive metabolic panel (CMP), and hepatitis B and C testing
- PET/CT scan and/or CT with contrast of chest, abdomen, and pelvis (C/A/T)
- Pregnancy test if chemotherapy or radiation therapy will be used

**Possible:**  
- Echocardiogram or MUGA scan
- Bone marrow biopsy with or without aspirate
- Endoscopy with multiple biopsies of sites (In cases where primary site is thought to be in head/neck or lungs, upper GI endoscopy should be considered)
- MRI with contrast or CT with contrast
- Autoimmune disease testing, particularly Sjögren syndrome
- Discussion of fertility issues and sperm banking
- SPEP blood test
Key points

- Extranodal marginal zone lymphoma (ENMZL) may be found in almost every part of the body.
- Typical non-gastric sites include the following: bowel (small and large), breast, head and neck, lung, around the eye (ocular adnexa), ovary, parotid, prostate, and salivary gland.
- Treatment is based on the exact location and extent of spread.
- Treatment options include surgery, radiation therapy, and chemoimmunotherapy depending on the location of the cancer and if it is early or advanced disease. Observation and clinical trials may also be considered.
- Your preferences about treatment are always important. Make your wishes known.

Those with marginal zone lymphoma should be treated at centers experienced in your type of cancer.
6
Nodal MZL

58 Overview
59 Testing
60 Treatment
61 Stages 1 and 2 (limited)
61 Stages 3 and 4 (advanced)
62 Follow-up care
62 Key points
Nodal marginal zone lymphoma (NMZL) forms in and is mostly limited to the lymph nodes. However, NMZL can be found outside of the lymph nodes in the bone marrow or blood. Together, you and your care team will choose a treatment plan that is right for you.

Overview

Nodal marginal zone lymphoma (NMZL) forms in and is mostly limited to the lymph nodes. However, NMZL can be found outside of the lymph nodes in the bone marrow or blood. Lymph nodes make immune cells that help the body fight infection. They also filter the lymph fluid and remove foreign material such as bacteria and cancer cells. Most are diagnosed with advanced-stage disease (stage 3 or 4). Almost everyone with NMZL has lymph nodes that are abnormal in size or consistency—called lymphadenopathy—at diagnosis, and many do not have symptoms (asymptomatic).

The lymph node

Nodal marginal zone lymphoma (NMZL) is found in the marginal zone area of the lymph node.
Testing

Nodal marginal zone lymphoma immunophenotype is usually CD10-, CD5-, CD20+, CD23-/+, CD43-/+, and cyclin D1-, and BCL2-.

Since this type of marginal lymphoma is uncommon. Testing is used to be distinguish NMZL from nodal follicular lymphoma (FL), mantle cell lymphoma (MCL), lymphoplasmacytic lymphoma (LPL), and chronic lymphocytic leukemia (CLL), all of which are more common.

Tests used to diagnose NMZL are found in Guide 7.

Guide 7
Tests to diagnose nodal marginal zone lymphoma (NMZL)

| Needed | • IHC panel: CD20, CD3, CD5, CD10, BCL2, kappa/lambda, CD21 or CD23, and cyclin D1 with or without cell surface marker analysis by flow cytometry: kappa/lambda, CD19, CD20, CD5, CD23, and CD10 |
| In some cases | • Biomarker testing to detect: immunoglobulin gene rearrangements, MYD88 mutation status to differentiate between Waldenström macroglobulinemia (WM) and marginal zone lymphoma, and PCR for t(11;18) • Karyotype or FISH: t(11;18), t(1;14), del(13q), del(7q) • FISH or PCR: t(14;18) |
Treatment

Since nodal MZL is most often a slow-growing disease, your care team might wait until symptoms appear before starting treatment. This is called active surveillance, observation, or “watch and wait.” During active surveillance, your care team will monitor for symptoms to appear. Once specific signs or symptoms appear, you will start treatment. Treatment options include radiation therapy, chemotherapy, immunotherapy, or a clinical trial. Involved-site radiation therapy (ISRT) treats cancer found in or near lymph nodes (nodal disease).

Tests used to plan treatment are found in Guide 8.

Guide 8
Tests to plan treatment

Biopsy, histology grading, and pathology review

Immunophenotyping with immunohistochemistry (IHC) and flow cytometry

Physical exam with performance status (PS)

Complete blood count (CBC) with differential, lactate dehydrogenase (LDH), comprehensive metabolic panel (CMP), and hepatitis B and C testing

PET/CT scan and/or CT with contrast of chest, abdomen, and pelvis (C/A/T)

Bone marrow biopsy with or without aspirate

Evaluation to rule out extranodal primary sites:
- Neck nodes: ocular, parotid, thyroid, and salivary gland
- Axillary nodes: lung, breast, and skin
- Mediastinal/hilar nodes: lung
- Abdominal nodes: splenic and GI
- Inguinal/iliac nodes: GI and skin

Pregnancy test if chemotherapy or radiation therapy will be used

Possible:
- Echocardiogram or MUGA scan
- Additional imaging
- Discussion of fertility issues and sperm banking
- SPEP blood test
Stages 1 and 2 (limited)

In stage 1, disease is found in one lymph node or in lymph node groups next to one another (contiguous).

In stage 2, disease is found in two or more lymph node groups on the same side of the diaphragm.

For stage 1 or contiguous stage 2 disease, treatment options include:

- ISRT (preferred)
- ISRT with anti-CD20 monoclonal antibody therapy. Chemotherapy might be added.
- Anti-CD20 monoclonal antibody therapy (rituximab or obinutuzumab) with or without chemotherapy

For non-contiguous stage 2 disease, treatment options include anti-CD20 monoclonal antibody (mAb) therapy. Chemotherapy and or radiation therapy (ISRT) might be added. Observation might be an option in some cases.

Stages 3 and 4 (advanced)

In stage 3, disease is found in lymph nodes on both sides of the diaphragm or in lymph nodes above the diaphragm and in the spleen.

In stage 4, disease is found in various areas outside of the lymph nodes.

Surveillance

Your care team might wait until certain signs or symptoms appear before starting treatment. This is called active surveillance or observation. During this time, you will have a physical exam and lab tests every 3 to 6 months for 5 years and then every year afterward. You will also have CT imaging scans with contrast no more than every 6 months. After 2 years, you will have a CT no more than once a year. Surveillance imaging is used for monitoring those without symptoms.

When to begin treatment

Treatment will likely start when you have any of the following:

- B symptoms (such as fever, night sweats, fatigue, and weight loss) and other symptoms similar to follicular lymphoma (FL)
- Threatened end-organ function (refers to damage occurring in major organs fed by the circulatory system such as the heart, kidneys, brain, and eyes)
- Low red blood cell count (cytopenia) not related to NMZL
- Bulky disease (single mass greater than 7 cm or 3 or more masses greater than 3 cm)
- Enlarged spleen (splenomegaly)
- Steady disease progression over at least 6 months

Treatment may include chemotherapy, immunotherapy, or a clinical trial.
Treatment response
For a complete response or remission (CR), observation or maintenance therapy is recommended for those treated with rituximab.

For a partial response (PR), the following is recommended:

- Observation
- Maintenance therapy for those treated with rituximab
- If you have had 3 or more lines of systemic therapy, then CAR T-cell therapy (axicabtagene ciloleucel) or a clinical trial

For no response or disease progression, you may have another biopsy and another round of systemic therapy with different agents (drugs) or a clinical trial could be considered. If you have had 3 or more lines systemic therapy, then CAR T-cell therapy (axicabtagene ciloleucel) might be given.

Follow-up care
After treatment, you will be monitored for relapse and disease progression. During this time, you will have a physical exam and lab tests every 3 to 6 months for 5 years and then every year afterward. You will also have CT scans with contrast no more than every 6 months. After 2 years, you will have a CT no more than once a year. Surveillance imaging is used for monitoring those without symptoms.

Key points
- Nodal marginal zone lymphoma (NMZL) forms in and is limited to the lymph nodes. However, NMZL can be found outside of the lymph nodes in the bone marrow or blood.
- Treatment options include radiation therapy, chemotherapy, immunotherapy, or a clinical trial.
- Since NMZL is most often a slow-growing disease, your care team might wait until symptoms appear before starting treatment. This is called active surveillance, observation, or “watch and wait.”
Splenic MZL

64 The spleen
65 Testing
66 Treatment
67 Recurrence
69 Key points
The spleen makes immune cells, filters the blood, stores blood cells, and removes old blood cells. Splenic marginal zone lymphoma (SMZL) is found in the blood, bone marrow, and spleen. The most common sign of SMZL is an enlarged spleen. Together, you and your care team will choose a treatment plan that is right for you.

The spleen

The spleen is a fist-sized organ located on the left side of the body near the stomach, pancreas, and just under the diaphragm. The spleen filters your blood of antigens (proteins) and microorganisms, and removes any old, damaged, or worn-out red blood cells. The spleen also contains infection-fighting white blood cells and controls the level of blood cells (white blood cells, red blood cells, and platelets) in the body.

The spleen is made up of 2 types of tissues: red pulp, which filters the blood, and white pulp, which contains white blood cells that regulate inflammation and the body’s response to infection.

Red pulp

Red pulp gives the spleen its red color. It is a loose spongy tissue that contains lymphocytes, macrophages, granulocytes, and plasma cells. The red pulp removes red blood cells—which carry oxygen—when they are old, damaged,
or infected. It harvests the iron from the old red blood cells for recycling into new blood cells.

**White pulp**

White pulp is all lymphatic (lymphoid) tissue. It is called white because it looks whiter than the surrounding red pulp. White pulp of the spleen has 3 sections: the periarteriolar lymphatic sheath (PALS), the follicles, and the marginal zone. The marginal zone is where the distribution of blood flow between slow and fast transit pathways is controlled.

**Marginal zone**

The marginal zone is the region at the intersection of the red pulp and white pulp of the spleen. Cancer of the B cells in this zone affects the movement of blood through the spleen.

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**Testing**

Splenic marginal zone lymphoma (SMZL) is the rarest type of marginal zone lymphoma. SMZL may be diagnosed by removal of the spleen (splenectomy), or by biopsy of the bone marrow and blood testing with imaging and other findings.

SMZL immunophenotype is usually CD10-, CD5-, CD20+, CD23/-+, CD43/-+, and cyclin D1-, BCL2- follicles, annexin A1, and CD103- (distinction from hairy cell leukemia) with expression of both IgM and IgD. NOTCH2 and KLF2 mutation status may be helpful to differentiate SMZL from other B-cell lymphoma subtypes.

Tests used to diagnose SMZL are found in Guide 9.

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**Guide 9**

**Tests to diagnose splenic marginal zone lymphoma (SMZL)**

<table>
<thead>
<tr>
<th>Needed</th>
<th>In some cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>• IHC panel: CD20, CD3, CD5, CD10, BCL2, kappa/lambda, CD21 or CD23,</td>
<td>• Biomarker testing to detect: immunoglobulin gene rearrangements, MYD88</td>
</tr>
<tr>
<td>cyclin D1, IgD, CD43, annexin A1 with or without cell surface marker</td>
<td>mutation status to differentiate between Waldenström macroglobulinemia (WM)</td>
</tr>
<tr>
<td>analysis by flow cytometry: kappa/lambda, CD19, CD20, CD5, CD23, CD10,</td>
<td>and marginal zone lymphoma (MZL), BRAF mutation status to differentiate</td>
</tr>
<tr>
<td>CD43, and CD103</td>
<td>MZL and hairy cell leukemia (HCL), and PCR for t(11;18)</td>
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<tr>
<td></td>
<td>• Karyotype or FISH: CLL panel; t(11;18), t(11;14), del(7q)</td>
</tr>
<tr>
<td></td>
<td>• FISH or PCR: t(14;18)</td>
</tr>
</tbody>
</table>
Treatment

Tests used to plan treatment are found in Guide 10.

Observation

Treatment can sometimes wait if:

- You have no pain, discomfort, or other symptoms (asymptomatic),
- Your spleen is not enlarged (splenomegaly), and
- Your low red blood cell count (cytopenia) is not getting worse.

Enlarged spleen

If you have an enlarged spleen (splenomegaly), you will be tested for hepatitis C (HCV). If you test positive for HCV, then it will be treated. If you continue to have symptoms and a low red blood cell count (cytopenia), then treatment with rituximab is preferred. Surgery to remove the spleen (splenectomy) is an option. Pneumococcal, meningococcal, haemophilus influenza, and hepatitis B vaccinations should be given at least 2 weeks before a splenectomy.

You can live a normal, healthy life without a spleen. However, your care team will try other

Guide 10

Tests to plan treatment

- Biopsy, histology grading, and pathology review
- Immunophenotyping with immunohistochemistry (IHC) and flow cytometry
- Physical exam with performance status (PS)
- Complete blood count (CBC) with differential, lactate dehydrogenase (LDH), comprehensive metabolic panel (CMP), and hepatitis B and C testing
- CT with contrast of chest, abdomen, and pelvis (C/A/T)
- Bone marrow biopsy with or without aspirate
- SPEP and/or immunoglobulin blood tests
- Pregnancy test if chemotherapy or radiation therapy will be used

Possible:
- PET/CT scan
- Additional imaging and specialized blood tests
- Discussion of fertility issues and sperm banking
Follow-up care
After treatment, you will be monitored for the return of cancer. During this time, you will have a physical exam with lab and imaging tests every 3 to 6 months for 5 years and then every year afterward.

Recurrence
Recurrence is the return of cancer.

Treatment will likely start when you have any of the following:

- Symptoms such as discomfort, pain, low blood cell counts, or difficulty breathing
- GI bleeding
- Threatened end-organ function
- Significant bulky disease
- Steady or rapid progression

Treatment will be systemic therapy, surgery to remove the spleen (splenectomy), or involved-site radiation therapy (ISRT).

If you did not have systemic therapy before, then you will be treated with first-line therapy. See Guide 11.

Guide 11
First-line therapy options

Preferred options
- Bendamustine with rituximab
- Cyclophosphamide, doxorubicin, vincristine, and prednisone with rituximab (RCHOP)
- Cyclophosphamide, vincristine, and prednisone (CVP) with rituximab
- Rituximab for those with splenic MZL or those who are older or unwell

Other recommended
- Lenalidomide with rituximab
- Rituximab for extranodal MZL and nodal MZL

For those who are older or unwell:
- Chlorambucil with or without rituximab
- Cyclophosphamide with or without rituximab

*Note: An FDA-approved biosimilar might be used for rituximab.
If you were previously treated with rituximab, then you will be treated with second-line therapy. See Guide 12.

### Guide 12

**Second-line and next-line therapy options**

<table>
<thead>
<tr>
<th>Preferred options</th>
<th>Other recommended</th>
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<tbody>
<tr>
<td>• Bendamustine with obinutuzumab or rituximab (not recommended if you had bendamustine before)</td>
<td>• Copanlisib for relapsed/refractory disease after 2 prior therapies</td>
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<tr>
<td>• Ibrutinib</td>
<td>• Rituximab</td>
</tr>
<tr>
<td>• Zanubrutinib</td>
<td>• Ibritumomab tiuxetan</td>
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<td>• Cyclophosphamide, doxorubicin, vincristine, and prednisone with rituximab (RCHOP)</td>
<td>• Cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP) with obinutuzumab</td>
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<td>• Cyclophosphamide, vincristine, and prednisone (CVP) with rituximab</td>
<td>• CVP with obinutuzumab</td>
</tr>
<tr>
<td>• Lenalidomide with rituximab</td>
<td>• Lenalidomide with obinutuzumab</td>
</tr>
<tr>
<td>• Rituximab</td>
<td></td>
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</tbody>
</table>

For those who are older or unwell:

- Chlorambucil with or without rituximab
- Cyclophosphamide with or without rituximab

*Note: An FDA-approved biosimilar might be used for rituximab.
Key points

- The spleen is the largest lymphatic organ. It makes immune cells, filters the blood, stores blood cells, and removes old blood cells.

- Splenic marginal zone lymphoma (SMZL) is found in the blood, bone marrow, and marginal zone of the spleen.

- Treatment can sometimes wait until you have symptoms, an enlarged spleen, and a worsening low red blood cell count.

- If you test positive for hepatitis C, then it will be treated before rituximab or surgery is considered.

- After treatment, you will be monitored for recurrence.

- Recurrence is the return of cancer. It is treated with systemic therapy, surgery to remove the spleen (splenectomy), or involved-site radiation therapy (ISRT).

Let us know what you think!

Please take a moment to complete an online survey about the NCCN Guidelines for Patients.

NCCN.org/patients/response
8
Transformed MZL

71 Overview
72 After little or no therapy
74 After multiple lines of therapy
76 Key points
Marginal zone lymphoma (MZL) can transform into diffuse large B-cell lymphoma (DLBCL). This means your slow-growing MZL has turned into a large-celled, fast-growing lymphoma. Together, you and your care team will choose a treatment plan that is right for you.

Overview

Marginal zone lymphoma (MZL) can transform into diffuse large B-cell lymphoma (DLBCL). This can occur before, during, or after treatment. In DLBCL, large-celled, fast-growing tumors are commonly found in lymph nodes, spleen, liver, bone marrow, or other tissues and organs.

Certain gene rearrangements can be found in DLBCL. In gene rearrangements, part of a gene has broken off and attached to another gene.

- *MYC, BCL2, and BCL6* gene rearrangements are commonly found in DLBCL.
- Double-hit B-cell lymphoma is a group of tumors with gene rearrangements involving at least 2 genes, including *MYC, BCL2, BCL6,* or other genes.
- Fluorescence in situ hybridization (FISH) will be done to look for gene rearrangements.

Get to know your care team and help them get to know you.

For more information, read *NCCN Guidelines for Patients: Diffuse Large B-Cell Lymphoma*, available at NCCN.org/patientguidelines.
### After little or no therapy

If MZL changed into DLBCL after little or no treatment, then it will be treated with a chemoimmunotherapy such as RCHOP. Radiation therapy might be given. Involved-site radiation therapy (ISRT) treats cancer found in or near lymph nodes (nodal disease).

RCHOP consists of rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone. For all systemic therapy options, see Guide 13.

#### Guide 13

**First-line therapy options**

<table>
<thead>
<tr>
<th>Preferred</th>
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<td>• Rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone</td>
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<tr>
<td>(RCHOP)</td>
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</tr>
<tr>
<td>• Dose-adjusted etoposide, prednisone, vincristine, cyclophosphamide,</td>
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</tr>
<tr>
<td>doxorubicin, and rituximab (DA-EPOCH-R)</td>
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</tr>
<tr>
<td>• Dose-adjusted etoposide, prednisone, vincristine, cyclophosphamide,</td>
<td></td>
</tr>
<tr>
<td>doxorubicin, and rituximab (DA-EPOCH-R)</td>
<td></td>
</tr>
<tr>
<td>• Rituximab, cyclophosphamide, liposomal doxorubicin (Doxil), vincristine,</td>
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</tr>
<tr>
<td>and prednisone (RCDOP)</td>
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<tr>
<td>• Rituximab, cyclophosphamide, etoposide, vincristine, and prednisone</td>
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</tr>
<tr>
<td>(RCEOP)</td>
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</tr>
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</tr>
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<td>(RCEPP)</td>
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<td>• Rituximab, cyclophosphamide, etoposide, prednisone, and procarbazine</td>
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<td>• Rituximab, gemcitabine, cyclophosphamide, vincristine, and prednisone</td>
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<tr>
<td>(RGCVP)</td>
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</table>

*Note: An FDA-approved biosimilar might be used for rituximab.*
**Treatment response**
After treatment, you will have imaging and lab tests to see if any cancer remains.

**Complete response**
In a complete response or remission (CR) no cancer remains. Observation or a clinical trial are options. If disease relapses, you will have a biopsy before treatment.

**Partial response**
If a partial response, you will have a different systemic therapy and can consider a hematopoietic cell transplant (HCT).

**No response or disease progress**
If your disease did not respond to treatment or has progressed, then a different systemic therapy will be given.
After multiple lines of therapy

If MZL changed into DLBCL after multiple lines of therapy, then the treatment recommendations include:

- Clinical trial
- Systemic therapy or CAR T-cell therapy. Options are based on previous drug therapy. A type of radiation therapy called involved-site radiation therapy (ISRT) might be added. ISRT treats cancer found in or near lymph nodes.
- Hematopoietic cell transplant (HCT)
- ISRT
- Best supportive care

For systemic therapy options, see Guide 14 and Guide 15.

The CAR T-cell therapy choice for transformation of all MZL subtypes is lisocabtagene maraleucel (Breyanzi).

CAR T-cell therapy options for transformation of nodal MZL include axicabtagene ciloleucel (Yescarta) and tisagenlecleucel (Kymriah).

Treatment response

After treatment, you will have imaging and blood tests to see if any cancer remains.

Complete response

In a complete response or remission (CR) no cancer remains. You might enter observation. A stem cell transplant such as autologous (self) hematopoietic cell transplant (autoHCT) or an allogeneic (donor) hemopoietic cell transplant (alloHCT) are also options in some cases. ISRT might be added. ISRT treats lymph nodes where cancer was originally found.

After treatment, you will enter surveillance and be monitored for relapse.

Partial response

In a partial response, treatment options are based on the types of treatment you had before. Options below depend on your individual situation:

- Allogeneic HCT in some cases. ISRT might be given.
- CAR T-cell therapy (if not previously given)
- ISRT
- Observation with monitoring

Relapse

If disease relapses, you will have a biopsy before treatment. Treatment might include a clinical trial, systemic therapy, radiation therapy, or best supportive care.

No response or disease progress

If disease has progressed, then best supportive care will be given. Best supportive care is given to improve quality of life and relieve discomfort.
### Guide 14

**Systemic therapy options: HCT planned**

<table>
<thead>
<tr>
<th>Preferred options</th>
<th>Rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone (RCHOP) if not previously given</th>
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<td></td>
<td>If previously treated with anthracycline-based regimen</td>
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<tr>
<td></td>
<td>• Dexamethasone and cytarabine (DHA) with carboplatin, cisplatin, or oxaliplatin (platinum-based chemotherapy).</td>
</tr>
<tr>
<td></td>
<td>• Gemcitabine, dexamethasone, and cisplatin (GDP) or gemcitabine, dexamethasone, and carboplatin</td>
</tr>
<tr>
<td></td>
<td>• Ifosfamide, carboplatin, and etoposide (ICE)</td>
</tr>
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</table>

*Note: Rituximab might be added to any of the therapies listed. An FDA-approved biosimilar might be used for rituximab.

### Guide 15

**Systemic therapy options: HCT not planned**

<table>
<thead>
<tr>
<th>Preferred options</th>
<th>Rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone (RCHOP) if not previously given</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>If previously treated with anthracycline-based regimen</td>
</tr>
<tr>
<td></td>
<td>• Gemcitabine and oxaliplatin (GemOx). Rituximab might be added.</td>
</tr>
<tr>
<td></td>
<td>• Polatuzumab vedotin-piiq. Bendamustine and/or rituximab might be added.</td>
</tr>
<tr>
<td></td>
<td>• Tafasitamab-cxix and lenalidomide</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Other recommended</th>
<th>• Cyclophosphamide, etoposide, vincristine, prednisone (CEOP). Rituximab might be added.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• Gemcitabine, dexamethasone, and cisplatin (GDP) or gemcitabine, dexamethasone, and carboplatin.</td>
</tr>
<tr>
<td></td>
<td>• Loncastuximab tesirine-lpyl</td>
</tr>
</tbody>
</table>

*Note: An FDA-approved biosimilar might be used for rituximab.
Key points

- Marginal zone lymphoma (MZL) can transform into diffuse large B-cell lymphoma (DLBCL). This means your slow-growing MZL has turned into a large-celled, fast-growing lymphoma.

- If MZL changed into DLBCL after little or no treatment, then it will be treated with a chemoimmunotherapy such as RCHOP. Radiation therapy might be given.

- If MZL changed into DLBCL after multiple lines of therapy, then the treatment recommendations include a clinical trial, systemic therapy or CAR T-cell therapy, radiation therapy, or best supportive care.

- A hematopoietic cell transplant (HCT) might be an option in some cases after multiple lines of therapy have been tried.
9
Making treatment decisions

78  It’s your choice
78  Questions to ask
88  Resources
It’s important to be comfortable with the cancer treatment you choose. This choice starts with having an open and honest conversation with your care team.

It’s your choice

In shared decision-making, you and your doctors share information, discuss the options, and agree on a treatment plan. It starts with an open and honest conversation between you and your doctor.

Treatment decisions are very personal. What is important to you may not be important to someone else.

Some things that may play a role in your decision-making:

- What you want and how that might differ from what others want
- Your religious and spiritual beliefs
- Your feelings about certain treatments like surgery or chemotherapy
- Your feelings about pain or side effects such as nausea and vomiting
- Cost of treatment, travel to treatment centers, and time away from school or work
- Quality of life and length of life
- How active you are and the activities that are important to you

Think about what you want from treatment. Discuss openly the risks and benefits of specific treatments and procedures. Weigh options and share concerns with your doctor.

If you take the time to build a relationship with your doctor, it will help you feel supported when considering options and making treatment decisions.

Second opinion

It is normal to want to start treatment as soon as possible. While cancer can’t be ignored, there is time to have another doctor review your test results and suggest a treatment plan. This is called getting a second opinion, and it’s a normal part of cancer care. Even doctors get second opinions!

Things you can do to prepare:

- Check with your insurance company about its rules on second opinions. There may be out-of-pocket costs to see doctors who are not part of your insurance plan.
- Make plans to have copies of all your records sent to the doctor you will see for your second opinion.

Support groups

Many people diagnosed with cancer find support groups to be helpful. Support groups often include people at different stages of treatment. Some people may be newly diagnosed, while others may be finished with treatment. If your hospital or community doesn’t have support groups for people with cancer, check out the websites listed in this book.

Questions to ask

Possible questions to ask your doctors are listed on the following pages. Feel free to use these questions or come up with your own. Be clear about your goals for treatment and find out what to expect from treatment.
Questions to ask about testing and diagnosis

1. What subtype and stage of marginal zone lymphoma do I have? What does this mean in terms of my prognosis and treatment options? Can this cancer be cured?

2. What tests do I need? What other tests do you recommend? How accurate are the tests?

3. How soon will I know the results and who will explain them to me?

4. Where will the tests take place? How long will the tests take?

5. Is there a cancer center or hospital nearby that specializes in my subtype of marginal zone lymphoma?

6. How do I prepare for testing?

7. Would you give me a copy of the pathology report and other test results?

8. Who will talk with me about the next steps? When?

9. Will I start treatment before the test results are in?

10. Will I have a biopsy? What type? What will be done to make me comfortable?

11. How often will I have blood tests?

12. How long will it take to get these test results?
Questions to ask your care team about their experience

1. What is your experience treating marginal zone lymphoma?

2. What is the experience of those on your team?

3. I would like a second opinion. Is there someone you can recommend? Who can help me gather all of my records for a second opinion?

4. I would like another pathologist or hematopathologist to review my blood samples. Is there someone you recommend?

5. How many patients like me (of the same age, gender, race) have you treated?

6. Will you be consulting with experts to discuss my care? Whom will you consult?

7. How many procedures like the one you’re suggesting have you done?

8. Is this treatment a major part of your practice?

9. How often is a complication expected? What are the complications?

10. Who will manage my day-to-day care?
Questions to ask about options

1. What will happen if I do nothing?
2. How do my age, overall health, and other factors affect my options?
3. What if I am pregnant? What if I'm planning to get pregnant in the near future?
4. Am I a candidate for a stem cell transplant?
5. Am I a candidate for a clinical trial? Can I join a clinical trial at any time?
6. Which option is proven to work best for my cancer, age, and other risk factors?
7. What are the possible complications and side effects?
8. Does any option offer long-term cancer control? Are the chances any better for one option than another? Less time-consuming? Less expensive?
9. What decisions must be made today? How long do I have to decide about treatment?
10. Is there a social worker or someone who can help me decide?
11. Is there a hospital or treatment center you can recommend for treatment? Can I go to one hospital for radiation therapy and a different center for systemic therapy?
Questions to ask about treatment

1. What are my treatment choices? What are the benefits and risks? Which treatment do you recommend and why?

2. Does the order of treatment matter?

3. Will I have to go to the hospital or elsewhere for treatment? How often? How long is each visit? Will I have to stay overnight in the hospital or make travel plans?

4. Do I have a choice of when to begin treatment? Can I choose the days and times of treatment? Should I bring someone with me?

5. Can I stop treatment at any time? What will happen if I stop treatment?

6. How much will this treatment cost me? How much will my insurance pay for this treatment? Are there any programs to help me pay for treatment?

7. Will I miss work or school? Will I be able to drive? When will I be able to return to my normal activities?

8. How will you know that treatment is working and how do you know if the treatment worked? How will I know?

9. What can be done to prevent or relieve the side effects of this treatment?

10. Are there any life-threatening side effects of this treatment? How will I be monitored?

11. What are the chances my cancer will return after this treatment? How will it be treated if it returns?

12. What are my chances of developing a different cancer later in life?
Questions to ask about radiation therapy

1. What type of radiation therapy (RT) will I have?

2. What will you target?

3. What is the goal of this RT?

4. How many treatment sessions will I require? Can you do a shorter course of RT?

5. Do you offer this type of RT here? If not, can you refer me to someone who does?

6. What side effects can I expect from RT?

7. Should I eat or drink before RT?

8. Will I be given medicine to help me relax during RT?

9. What should I wear?
Questions to ask about surgery

1. What will be removed during surgery? What will this mean in terms of my recovery?

2. What kind of surgery will I have? Will I have more than one surgery?

3. Does my cancer involve any veins or arteries? How might this affect surgery?

4. How long will it take me to recover from surgery? When will I be able to return to work?

5. How much pain will I be in? What will be done to manage my pain?

6. What is the chance that this surgery will shorten my life?

7. What other side effects can I expect from surgery? What complications can occur from this surgery? If I don’t have surgery, what are my chances of survival?

8. What treatment will I have before, during, or after surgery? What does this treatment do?
Questions to ask about side effects

1. What are the side effects of treatment?

2. What are the side effects of marginal zone lymphoma?

3. How long will these side effects last? Do any side effects lessen or worsen in severity over time?

4. What side effects should I watch for? What side effects are expected and which are life threatening?

5. When should I call the doctor? Can I text? What should I do on weekends and during non-office hours?

6. What emergency department or ER should I go to? Will my treatment team be able to communicate with the ER team?

7. What medicines can I take to prevent or relieve side effects?

8. Will you stop treatment or change treatment if there are side effects? What do you look for?

9. What can I do to lessen or prevent side effects? What will you do?

10. What medicines may worsen side effects of treatment?

11. What are some of the likely permanent side effects that I might have from the treatment?
Questions to ask about clinical trials

1. What clinical trials are available for my type of cancer? Are they at your center or office? If they are not at your center or office, will you still follow my care during and after the trial?

2. What are the treatments used in the clinical trial?

3. What does the treatment do?

4. Has the treatment been used before? Has it been used for other types of lymphoma?

5. What are the risks and benefits of this treatment?

6. What side effects should I expect? How will the side effects be controlled?

7. How long will I be in the clinical trial?

8. Will I be able to get other treatments if this doesn't work?

9. How will you know the treatment is working?

10. Will the clinical trial cost me anything? If so, how much?

11. How do I find out about clinical trials that I can participate in? Are there online sources that I can search?
Questions to ask about hematopoietic cell transplants

1. Which type of transplant is an option for me?
2. What do I need to do to prepare?
3. What will you do to prepare?
4. What are the risks to myself and/or the donor?
5. How will the transplant affect my prognosis?
6. How will a transplant affect the quality and length of my life?
7. What should I expect from a transplant?
8. How long should I expect to be in the hospital?
9. How will I feel before, during, and after the transplant?
10. How many transplants has this center done for my subtype of marginal zone lymphoma?
11. What is my risk of developing graft-versus-host disease?
### Resources

<table>
<thead>
<tr>
<th>Organization</th>
<th>Website</th>
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<tbody>
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<td>American Association for Cancer Research (AACR)</td>
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<td>Be The Match®</td>
<td><a href="http://bethematch.org">bethematch.org</a></td>
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<td>Blood &amp; Marrow Transplant Information Network (BMT InfoNet)</td>
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<table>
<thead>
<tr>
<th>Other Resources</th>
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</thead>
<tbody>
<tr>
<td>My Survival Story</td>
<td><a href="http://mysurvivalstory.org">mysurvivalstory.org</a></td>
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<td>National Bone Marrow Transplant Link</td>
<td><a href="http://nbmtlink.org">nbmtlink.org</a></td>
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<td>National Coalition for Cancer Survivorship</td>
<td><a href="http://canceradvocacy.org/toolbox">canceradvocacy.org/toolbox</a></td>
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<td>National Hospice and Palliative Care Organization</td>
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<td>Patient Access Network Foundation</td>
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<td>Radiological Society of North America</td>
<td><a href="http://radiologyinfo.org">radiologyinfo.org</a></td>
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<td>Testing.com</td>
<td><a href="http://testing.com">testing.com</a></td>
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</table>
Words to know

allogeneic stem cell transplant (alloSCT)
A cancer treatment that replaces abnormal blood stem cells with healthy donor cells.

autologous stem cell transplant (autoSCT)
A cancer treatment that destroys your bone marrow then rebuilds it with your healthy stem cells. Also called high-dose therapy with autologous stem cell rescue (HDT/ASCR).

best supportive care
Treatment to improve quality of life and relieve discomfort.

biomarker testing
A lab test of any molecule in your body that can be measured to assess your health. Also called molecular testing.

biopsy
A procedure that removes fluid or tissue samples to be tested for a disease.

biosimilar
A drug that is almost an identical drug made by another company. It has been approved by the U.S. Food and Drug Administration (FDA) and must be used in the exact same way and at the same dose as the other drug.

bone marrow
The sponge-like tissue in the center of most bones.

bone marrow aspiration
A procedure that removes a liquid bone marrow sample to test for a disease.

bone marrow biopsy
A procedure that removes bone and solid bone marrow samples to test for a disease.

chemotherapy
Cancer drugs that stop the cell life cycle so that cells don’t increase in number.

chromosome
The structures within cells that contain coded instructions for cell behavior.

clinical trial
A type of research that assesses health tests or treatments.

complete blood count (CBC)
A lab test that includes the number of blood cells.

complete response (CR)
No signs of lymphoma are found. Also called complete remission.

comprehensive metabolic panel (CMP)
Tests up to 14 chemicals in your blood.

computed tomography (CT)
A test that uses x-rays from many angles to make a picture of the insides of the body.

contrast
A substance put into your body to make clearer pictures during imaging tests.

core needle biopsy
A procedure that removes tissue samples with a hollow needle. Also called core biopsy.

cytogenetics
The study of chromosomes using a microscope.

deoxyribonucleic acid (DNA)
A chain of chemicals in cells that contains coded instructions for making and controlling cells.

differential
A lab test of the number of white blood cells for each type.
endoscope
A thin, long tube fitted with tools that is guided down the mouth.

fine-needle aspiration (FNA)
A procedure that removes tissue samples with a very thin needle.

flow cytometry
A lab test of substances on the surface of cells to identify the type of cells present.

fluorescence in situ hybridization (FISH)
A lab test that uses special dyes to look for abnormal chromosomes and genes.

gastroenterologist
A doctor who’s an expert in digestive diseases. This system contains organs that break down food for the body to use.

gastrointestinal (GI) tract
The group of organs through which food passes after being eaten. Also called digestive tract.

gene
A set of coded instructions in cells for making new cells and controlling how cells behave.

H. pylori
A type of bacterium that causes inflammation and ulcers in the stomach or small intestine. People with H. pylori infections may be more likely to develop cancer in the stomach, including extranodal marginal zone lymphoma (ENMZL). Also called Helicobacter pylori.

hematopathologist
A doctor who specializes in the study of blood diseases and cancers using a microscope.

hematopoietic cell transplant (HCT)
A cancer treatment that replaces abnormal blood stem cells with healthy cells. Also called stem cell transplant (SCT) or bone marrow transplant (BMT).

histology
The study of tissues and cells under a microscope.

human leukocyte antigen (HLA)
A cell protein by which your body knows its own cells from foreign cells.

imaging test
A test that makes pictures (images) of the insides of the body.

immune system
The body’s natural defense against infection and disease.

immunohistochemistry (IHC)
A lab test of cancer cells to find specific cell traits involved in abnormal cell growth.

immunophenotyping
A lab test that detects the type of cells present based on the cells’ surface proteins.

induction
The first treatment that is given to greatly reduce the amount of cancer.

involved-site radiation therapy (ISRT)
Uses radiation therapy to treat cancer found in or near lymph nodes (nodal disease).

karyotype
Lab test that makes a map of chromosomes to find defects.

lactate dehydrogenase (LDH)
A protein in blood that helps to make energy in cells.

lymph
A clear fluid containing white blood cells.

lymph node
A small, bean-shaped disease-fighting structure.
lymphadenopathy
Lymph nodes that are abnormal in size or consistency.

lymphatic system
Germ-fighting network of tissues and organs that includes the bone marrow, spleen, thymus, lymph nodes, and lymphatic vessels. Part of the immune system.

lymphedema
Swelling in the body due to a buildup of fluid called lymph.

magnetic resonance imaging (MRI)
A test that uses radio waves and powerful magnets to make pictures of the insides of the body.

monitoring
A period of testing for changes in cancer status.

morphology
The science of the form and structure of organisms.

mutation
An abnormal change in the instructions within cells for making and controlling cells.

partial response
Lymphoma is still present, but has reduced in size.

pathologist
A doctor who’s an expert in testing cells and tissue to find disease.

peripheral blood (PB)
Blood that circulates throughout the body.

platelet (PLT)
A type of blood cell that helps control bleeding. Also called thrombocyte.

polymerase chain reaction (PCR)
A lab process in which copies of a DNA part are made.

positron emission tomography (PET)
A test that uses radioactive material to see the shape and function of body parts.

prognosis
The pattern and outcome of a disease.

radiation therapy (RT)
A treatment that uses high-energy rays.

recovery
A period of time without treatment to allow blood cell counts to return to normal.

recurrence
The return of cancer after a cancer-free period.

red blood cell
A type of blood cell that carries oxygen from the lungs to the rest of the body. Also called an erythrocyte.

refractory cancer
A cancer that does not improve with treatment.

relapse
The return or worsening of cancer after a period of improvement.

side effect
An unhealthy or unpleasant physical or emotional response to treatment.

spleen
An organ that is part of the lymphatic system. The spleen makes lymphocytes, filters the blood, stores blood cells, and destroys old blood cells. It is located on the left side of the abdomen near the stomach.

splenectomy
Surgery to remove the spleen.
**Words to know**

**stem cell transplant (SCT)**
A cancer treatment that replaces abnormal blood stem cells with healthy cells. Also called hematopoietic cell transplant (HCT) or bone marrow transplant (BMT).

**supportive care**
Treatment for the symptoms or health conditions caused by cancer or cancer treatment. Also sometimes called palliative care or best supportive care.

**translocation**
A switching of parts between two chromosomes.

**tumor lysis syndrome (TLS)**
A condition caused when waste released by dead cells is not quickly cleared out of your body.

**white blood cell (WBC)**
A type of blood cell that helps fight infections in the body. Also called a leukocyte.
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