

Understanding Marginal Zone Lymphoma

Marginal zone lymphomas (MZLs) are a group of indolent (slow-growing) B-cell non-Hodgkin lymphomas (NHLs), which account for approximately five to ten percent of all NHL cases. The average age at diagnosis is about 60 years, and they are slightly more common in women than in men.

TYPES OF MZL

EXTRANODAL MZL OR MUCOSA-ASSOCIATED LYMPHOID TISSUE (MALT) LYMPHOMA

Extranodal MZL or mucosa-associated lymphoid tissue (MALT) lymphoma is the most common form of MZL, accounting for about 60 to 70 percent of all MZL cases per year and about five percent of all NHLs. This type occurs outside the lymph nodes in places such as the stomach, breast, small intestine, salivary gland, thyroid, structures around the eyes (ocular adnexa), and lungs. MALT lymphoma is divided into two categories: *gastric*, which develops in the stomach and is the most common site, and *non-gastric*, which develops outside of the stomach.

In many cases of MALT lymphoma, the patient has a previous medical history of chronic infection, inflammation, or autoimmune disorders at the affected organ. For example, *Helicobacter pylori* (*H. pylori*), a bacteria linked to chronic stomach irritation, has been associated with the vast majority of patients with gastric MALT lymphoma.

NODAL MZL

Nodal MZL occurs within the lymph nodes and accounts for about 30 percent of all MZL cases.

SPLENIC MZL

Splenic MZL occurs most often in the spleen, blood, and bone marrow. It has been associated with hepatitis C virus (HCV) infection. Splenic MZL comprises just under ten percent of MZL cases diagnosed each year.

TREATMENT OPTIONS

Treatment selection for a patient with MZL depends on the type, the stage and location of the disease, the patient's age and overall health, and any lymphoma-related signs or symptoms.

GASTRIC MALT LYMPHOMAS

Since gastric MALT lymphoma is often the result of an infection with *H. pylori*, the initial treatment is a triple therapy of two antibiotics combined with proton pump inhibitors (PPIs), typically given for two weeks. PPIs reduce the production of stomach acid to help prevent or heal ulcers. In about 90 percent of cases, these lymphomas go away following antibiotic and PPI treatment, although this may take several months. Most gastric MALT lymphomas are low-grade lesions that grow slowly and do not tend to spread to other places in the body. If the lymphoma *relapses* (disease returns after treatment) or becomes *refractory* (does not respond to treatment) after triple therapy, there are many additional treatment options available, including radiation or monoclonal antibodies targeting CD20 such as rituximab (Rituxan), alone or in combination with chemotherapy.

NON-GASTRIC MALT LYMPHOMAS

Non-gastric MALT lymphoma can appear in a variety of areas throughout the body. Therefore, treatment is usually based on the exact location and extent of spread. Physicians may defer treatment until symptoms appear, an approach called *active surveillance*, also known as *watchful waiting* (observation with no drug or radiation therapy given). With this strategy,

patients' overall health and disease are monitored through regular checkup visits and various evaluating procedures, such as laboratory and imaging tests. Active treatment is started if the patient begins to develop lymphoma-related symptoms or there are signs that the disease is progressing based on testing during follow-up visits. In localized cases, treatment typically includes radiation therapy. In rare cases where radiation is not feasible, surgery can be used as an alternative. More advanced disease is usually treated with immunotherapy such as the monoclonal antibody rituximab (Rituxan), with or without chemotherapy. Common initial chemotherapy combination treatments are bendamustine (Treanda) plus rituximab (BR) or R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone), which are used to treat other slow-growing lymphomas such as follicular lymphoma. The antibiotic doxycycline has been shown to be effective in MZL that affects the area around the eye (ocular adnexal lymphoma [OAL]) in certain areas of the world where infection with *Chlamydia psittaci* is commonly associated with OAL.

NODAL MZL

Because nodal MZL is most often a slow-growing disease, physicians may adopt an active surveillance or watchful waiting approach until symptoms appear. When treatment is necessary, options include radiation therapy, chemotherapy and/or immunotherapy, and other treatments commonly used in other types of slow-growing lymphomas, such as follicular lymphoma.

SPLENIC MZL

Treatment is not always immediately necessary for splenic MZL. When treatment is deemed appropriate, several options exist. Some patients may receive a *splenectomy* (surgical removal of the spleen); patients ineligible for surgery may receive low-dose radiation of the spleen. Other patients may be given rituximab (Rituxan) with or without chemotherapy. In some cases, because of the association of this type of lymphoma with HCV, treatment of the HCV infection might result in the resolution of the lymphoma.

New treatments for all subtypes have been recently approved for relapsed disease. Ibrutinib (Imbruvica) was the first drug to be specifically approved by the U.S. Food and Drug Administration (FDA) for the treatment of MZL in these circumstances. It is used for the treatment of patients with MZL who require *systemic* (throughout the body) therapy and have received at least one prior anti-CD20-based therapy. Lenalidomide (Revlimid), is another oral medication that has been recently approved by the FDA for the treatment of patients with MZL who have received at least one prior therapy, and it is used in combination with rituximab (Rituxan), often referred to as R2 (R-squared).

For all subtypes, *biosimilar therapies* (drugs that are modeled after an existing biologic therapy) may be an option for patients who are taking rituximab. These include rituximab-abbs and rituximab-pvvr. For more information, patients should view the *Biosimilars* fact sheet on LRF's website at lymphoma.org/publications and talk to their physician.



TREATMENTS UNDER INVESTIGATION

Several new drugs and drug combinations are being studied in clinical trials for MZL and other slow-growing lymphomas, including:

- Alisertib
- Axicabtagene ciloleucel (Yescarta)
- Blinatumomab (Blincyto)
- Bortezomib (Velcade)
- Buparlisib
- Carfilzomib (Kyprolis)
- Copanlisib (Aliqopa)
- Entospletinib
- Idelalisib (Zydelig)
- Ixazomib (Ninlaro)
- Nivolumab (Opdivo)
- Obinutuzumab (Gazyva)
- Panobinostat (Farydak)
- Pembrolizumab (Keytruda)
- Ublituximab
- Umbralisib
- Venetoclax (Venclexta)

It is critical to remember that today's scientific research is continuously evolving. Treatment options may change as new treatments are discovered and current treatments are improved. Therefore, it is important that patients check with their physician or with the Lymphoma Research Foundation (LRF) for any treatment updates that may have recently emerged.



CLINICAL TRIALS

Clinical trials are crucial in identifying effective drugs and determining optimal doses for patients with lymphoma. Patients interested in participating in a clinical trial should view the *Understanding Clinical Trials* fact sheet on LRF's website at lymphoma.org/publications and the *Clinical Trials Search Request Form* at lymphoma.org, talk to their physician, or contact the LRF Helpline for an individualized clinical trial search by calling (800) 500-9976 or emailing helpline@lymphoma.org.

FOLLOW-UP

Patients with lymphoma should have regular visits with a physician who is familiar with their medical history and the treatments they have received. Medical tests (such as blood tests, computed tomography [CT] scans, and positron emission tomography [PET] scans) may be required at various times during remission to evaluate the need for additional treatment.

Some treatments can cause long-term side effects or late side effects, which can vary based on the duration and frequency of treatments, age, gender, and the overall health of each patient at the time of treatment. A physician will check for these side effects during follow-up care. Visits may become less frequent the longer the disease remains in remission.

Patients and their caregivers are encouraged to keep copies of all medical records and test results, as well as information on the types, amounts, and duration of all treatments received. This documentation will be important for keeping track of any side effects resulting from treatment or potential disease recurrences. LRF's award-winning *Focus On Lymphoma* mobile app (lymphoma.org/mobileapp) can help patients manage this documentation.

PATIENT AND CAREGIVER SUPPORT SERVICES

A lymphoma diagnosis often triggers a range of feelings and concerns. In addition, cancer treatment can cause physical discomfort. LRF's *Lymphoma Support Network* connects patients and caregivers with volunteers who have experience with MZL and similar treatments or challenges, for mutual emotional support and encouragement. Patients and loved ones may find this information useful whether the patient is newly diagnosed, in treatment, or in remission.

Contact LRF:
Helpline: (800) 500-9976
Email: helpline@lymphoma.org
www.lymphoma.org

Medical reviewer:
Francesca Montanari, MD
Columbia University Medical Center

Supported through grants from:



The *Understanding Lymphoma* series is published by the Lymphoma Research Foundation (LRF) for the purpose of informing and educating readers. Facts and statistics were obtained using published information, including data from the Surveillance, Epidemiology, and End Results (SEER) Program. Because each person's body and response to treatment is different, no individual should self-diagnose or embark upon any course of medical treatment without first consulting with his or her physician. The medical reviewer, the medical reviewer's institution, and LRF are not responsible for the medical care or treatment of any individual.

© 2020 Lymphoma Research Foundation

Last updated 2020

Resources

LRF offers a wide range of resources that address treatment options, the latest research advances, and ways to cope with all aspects of MZL, including our award-winning mobile app. LRF also provides many educational activities, from in-person meetings to webinars, for people with MZL, as well as patient guides and e-Updates that provide the latest disease-specific news and treatment options. To learn more about any of these resources, visit our websites at lymphoma.org/MZL or lymphoma.org, or contact the LRF Helpline at (800) 500-9976 or helpline@lymphoma.org.