

Mantle cell lymphoma (MCL) is a rare type of B-cell non-Hodgkin lymphoma (NHL). It can occur in men and women of any age, but it most commonly affects men over 60 years old. MCL comprises about 5% of all NHLs and it often starts out in a more *indolent* (slow-growing) manner but can become more *aggressive* (fast-growing) over time.

The disease is called “mantle cell lymphoma” because the tumor cells come from white blood cells (B-lymphocytes) that are found in the “mantle zone” of the lymph nodes (small bean-shaped structures that help the body fight infection, Figure 1). By the time a person is diagnosed, it is very common that the disease is found in other sites like lymph nodes, spleen, bone marrow (the spongy tissue inside the bone), and gastrointestinal tract.

For more information on diagnosis and disease staging of relapsed and refractory MCL, please view the *Understanding Lymphoma and CLL Guide* on the Foundation’s website (visit lymphoma.org/publications).

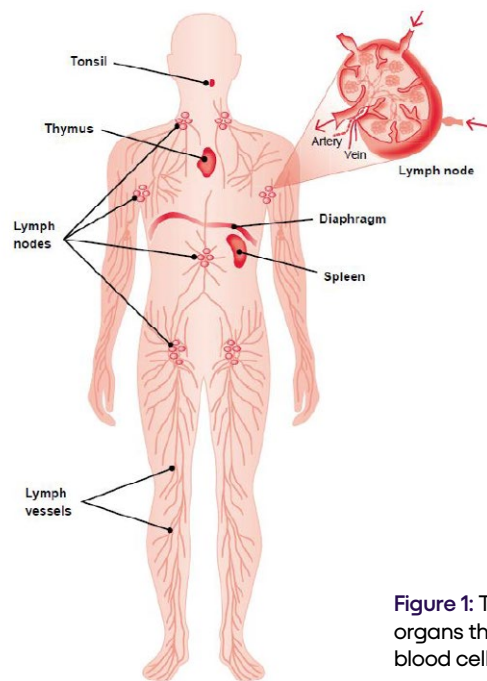


Figure 1: The lymphatic system (tissues and organs that produce, store, and carry white blood cells) and lymph nodes.

Symptoms

Some patients with MCL do not have any symptoms. Other patients may develop swollen lymph nodes (usually painless) in the neck, armpit or groin.

Some patients who do not have symptoms and who have a small volume of slow-growing disease at diagnosis may not need treatment right away. This approach is referred to as *active surveillance* (also known as “watchful waiting” or “observation”) and includes monitoring patients’ overall health and disease through regular physical exams (to check for any swollen lymph nodes) or periodic imaging tests (like computed tomography [CT] scans). If patients begin to have symptoms or signs of disease progression, treatment is initiated. To know more about active surveillance, view *Active Surveillance* fact sheet on the Lymphoma Research Foundation’s website at lymphoma.org/publication.

In patients who require treatment, MCL usually responds well to *first-line* (initial) therapies. How long each patient stays in remission (no signs of cancer) may be different depending on the type of MCL (indolent or aggressive) and the kind of treatment given. MCL is a chronic heterogenous (with different characteristics across patients) disease where most patients will need treatment more than one time.

Treatment Options

There is a growing number of treatment options for the management of relapsed (returned after treatment) or *refractory* (does not respond to treatment) MCL. The type of treatment recommended depends on:

- Treatments already received
- When the relapse happened
- The patient's age and overall health

The treatment types that have been approved by the U.S. Food and Drug Administration (FDA) for the treatment of relapsed or refractory MCL include:

- Targeted therapies (drugs that target molecules that cancer cells use to grow and spread). This includes inhibitors of proteins involved in cell signaling and growth like kinases (such as acalabrutinib [Calquence], zanubrutinib [Brukinsa], and pirtobrutinib [Jaypirca]) and proteasome inhibitors such as bortezomib (Velcade).
- Immunotherapy (drugs that use the body's immune system to fight cancer), including:
 - Immunomodulatory drugs that work on the immune system directly by regulating (activating or slowing down) the activity of specific proteins, such as lenalidomide (Revlimid).
 - Chimeric antigen receptor (CAR) T cell therapies (a special type of immunotherapy that uses the patient's immune cells to fight cancer), such as brexucabtagene autoleucl (Tecartus).

Most of the drugs mentioned above may be used in combination with a monoclonal antibody (protein made in the laboratory that binds to cancer cells and help the immune system destroy them) called rituximab (Rituxan) or rituximab biosimilars (like rituximab-abbs and rituximab-pvvr). Biosimilars are drugs that are modeled after a biologic therapy (a molecule produced inside a living cell) that already exists and is approved for use. To learn more, please see the *Biosimilar Therapies* factsheet on the Lymphoma Research Foundation's website at lymphoma.org/publications.

Additional treatment types that may be used in relapsed/refractory MCL include:

- Chemotherapy (drugs that stop the growth of or kill cancer cells), such as bendamustine (Treanda) with or without rituximab (Rituxan), and combination chemotherapy with or without rituximab (Rituxan).
- Stem cell transplantation (SCT, the patient is treated with high-dose chemotherapy or radiation to remove their blood-forming cells or stem cells, and then receives healthy stem cells to restore the immune system and the bone marrow's ability to make new blood cells).
 - Autologous SCT (the patient's own stem cells are used)
 - Allogeneic SCT (patients receive stem cells from another donor)

Autologous SCT is generally given after a patient's first therapy, but it may also work well for medically fit patients who have a good response to later therapies. Younger medically fit patients may consider allogeneic SCT as a possible cure, although it may have more risks. Patients should discuss with their doctor the benefits and risks of SCT. For more information on transplantation, see the *Understanding Cellular Therapy* guide (visit lymphoma.org/publications).

Treatments Under Investigation

Many new treatments (also referred to as investigational drugs) and combinations are currently being tested in clinical trials for patients with relapsed or refractory MCL. Results from these clinical trials may improve or change the current standard of care (the proper treatment that is widely used by healthcare professionals and accepted by medical experts). **Table 1** (below) lists some of these investigational drugs that can be accessed through a clinical trial. For more information on clinical trials, view the *Understanding Clinical Trials* publication on the Lymphoma Research Foundation's website at lymphoma.org/publication.

Table 1: Treatments Under Investigations for Relapsed/Refractory Mantle Cell Lymphoma

Agent (drug)	Class (type of treatment)
Carfilzomib (Kyprolis)	Targeted therapy; proteasome inhibitor
Cirmtuzumab (UC-961)	Immunotherapy; monoclonal antibody, anti-ROR1
Ixazomib (Ninlaro)	Targeted therapy; proteasome inhibitor
Loncastuximab tesirine (Zynlonta)	Antibody-drug conjugate; anti-CD19
Mosunetuzumab (Lunsumio)	Immunotherapy; bispecific antibody
MS-553	Targeted therapy; PI3Kδ inhibitor
Nemtabrutinib (MK-1026, ARQ 531)	Targeted therapy; BTK inhibitor
Nivolumab (Opdivo)	Immune checkpoint inhibitor; anti-PD-1 receptor
Obinutuzumab (Gazyva)	Immunotherapy; monoclonal antibody, anti-CD20
Odronextamab (REGN1979)	Immunotherapy; bispecific antibody
Palbociclib (Ibrance)	Targeted therapy; CDK inhibitor
Parsaclisib (INCB050465)	Targeted therapy; PI3Kδ inhibitor
Polatuzumab vedotin (Polivy)	Immunotherapy; antibody-drug conjugate
Relmacabtagene autoleucl (JWCAR029)	Autologous CAR T cell; anti-CD19
Venetoclax (Venclexta)	Targeted therapy; BCL2 inhibitor
Zilovertamab vedotin (MK-2140)	Immunotherapy; antibody-drug conjugate

BCL2, B-cell lymphoma 2 protein; BTK, Bruton tyrosine kinase; CAR, chimeric antigen receptor; CDK, cyclin-dependent kinases; PD-1, programmed cell death protein 1; PI3K, phosphoinositide 3-kinase; ROR1, receptor tyrosine kinase like orphan receptor 1.

Treatment choices are increasing as new drugs are developed and current treatments are improved. Because science is always changing, it is important for patients to check in with their oncologist or hematologist specialized in MCL or with the Foundation to find out about any new treatments that become available. It is also very important that all patients with MCL consult their doctor to clear up any questions.

Clinical Trials

Clinical trials are crucial in identifying effective drugs and the best treatment doses for patients with relapsed or refractory MCL. Because the optimal initial treatment of MCL is not clear and it is such a rare disease, clinical trials enrollment is important for establishing more effective and less toxic treatments. The rarity of the disease also means that the latest treatments are often available only through clinical trials. Patients interested in participating in a clinical trial should view the *Understanding Clinical Trials* factsheet on the Foundation's website (visit lymphoma.org/publications), talk to their physician, or contact the Helpline for an individualized clinical trial search by calling (800) 500-9976 or emailing helpline@lymphoma.org.

Follow-up

Patients with relapsed or refractory MCL should have regular visits with their physician. During these visits, medical tests (such as blood tests, computed tomography [CT] scans, and positron emission tomography [PET] scans) may be required to evaluate the need for additional treatment. Periodically, it may be necessary to repeat a tumor biopsy (removing a small piece of the tumor to look at the cancer cells under the microscope) to better understand the biology of the lymphoma.

Some treatments can cause long-term side effects (occur **during** treatment and continue for months or years) or late side effects (appear only months, years or decades **after** treatment has ended).

These side effects can vary depending on the following factors:

- Duration of treatment (how long the treatment lasted)
- Frequency of treatment (how often was the treatment administered)
- Type of treatment given
- Age and gender of the patient
- Patient overall health 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 care partners are encouraged to keep copies of all medical records. These include test results as well as information on the types, amounts, and duration of all treatments received. Medical records are important for keeping track of any side effects resulting from treatment or potential disease recurrences. The Foundation's award-winning **Focus On Lymphoma** mobile app (lymphoma.org/mobileapp) and the *Lymphoma Care Plan* (lymphoma.org/publications) can help patients manage this documentation.

Lymphoma Care Plan

Keeping your information in one location can help you feel more organized and in control. This also makes it easier to find information pertaining to your care and saves valuable time. The Foundation's Lymphoma Care Plan document organizes information on your health care team, treatment regimen, and follow-up care. You can also keep track of health screenings and any symptoms you experience to discuss with your health care provider during future appointments. The Lymphoma Care Plan document can be accessed by visiting lymphoma.org/publications.

Patient Education Programs

The Foundation also offers a variety of educational activities, including live meetings and webinars for individuals looking to learn directly from lymphoma experts. These programs provide the lymphoma community with important information about the diagnosis and treatment of lymphoma, as well as information about clinical trials, research advances and how to manage/cope with the disease. These programs are designed to meet the needs of a lymphoma patient from the point of diagnosis through long-term survivorship. To view our schedule of upcoming programs, please visit lymphoma.org/programs.

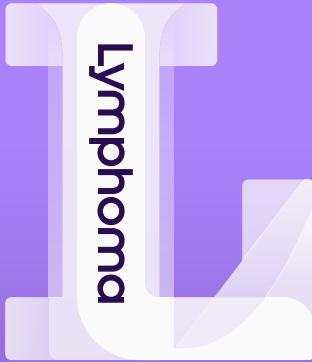
Helpline

The Foundation's Helpline staff are available to answer your general questions about lymphoma and treatment information, as well as provide individual support and referrals to you and your loved ones. Callers may request the services of a language interpreter. The Foundation also offers a one-to-one peer support program called the Lymphoma Support Network and clinical trials information through our Clinical Trials Information Service. For more information about any of these resources, visit our website at lymphoma.org, or contact the Helpline at (800) 500-9976 or helpline@lymphoma.org.

Para información en Español, por favor visite lymphoma.org/es. (For Information in Spanish please visit lymphoma.org/es).

Focus on Lymphoma Mobile App

Focus on Lymphoma is the first app to provide patients and their care partners with tailored content based on lymphoma subtype, and actionable tools to better manage diagnosis and treatment. Comprehensive lymphoma management, conveniently in one secure and easy-to-navigate app, no matter where you are on the care continuum. Get the right information, first, with resources from the entire Lymphoma Research Foundation content library, use unique tracking and reminder tools, and connect with a community of specialists and patients. To learn more about this resource, visit our website at lymphoma.org/mobileapp, or contact the Foundation's Helpline at (800) 500-9976 or helpline@lymphoma.org.



Research Foundation

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