LYMPHOMA
RESEARCH • FOUNDATION

Understanding Lymphoma: Mantle Cell Lymphoma

Mantle cell lymphoma (MCL) is a rare B-cell non-Hodgkin lymphoma (NHL) that most often affects men over the age of 60. MCL represents about 5% of all NHLs, and it often starts out as an indolent (slow-growing) disease but can become more aggressive (fast-growing) over time.

The disease is called "mantle cell lymphoma" because the tumor cells originally come from the "mantle zone" of lymph node (small bean-shaped structures that help the body fight disease; Figure 1). In addition to being found in lymph nodes, MCL is often present in the spleen, gastrointestinal tract (digestive system, which includes the esophagus, stomach, and intestines), bone marrow (the spongy tissue inside the bone), bloodstream, and other sites at the time of diagnosis.

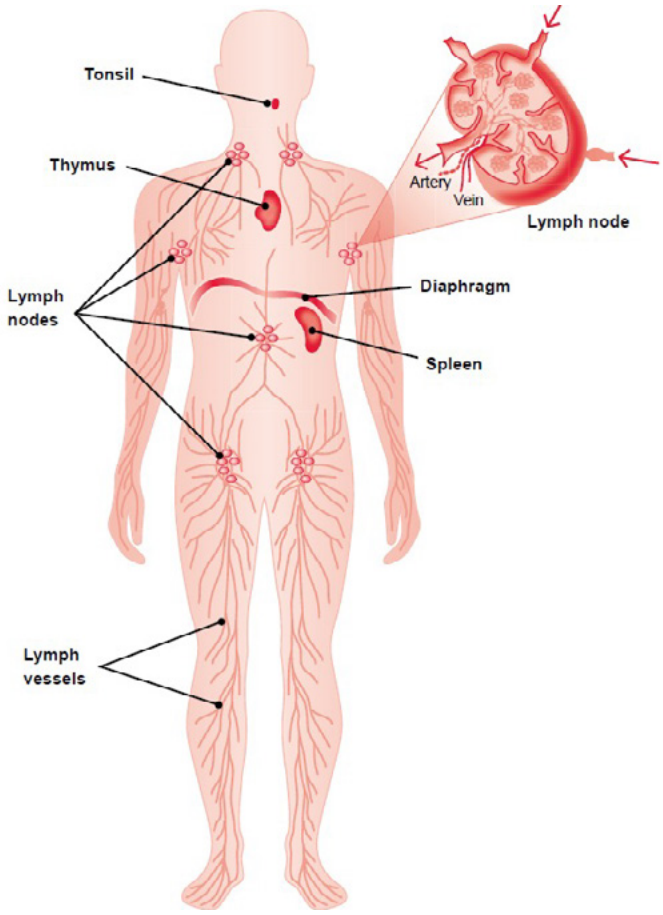

Figure 1. The lymphatic system (tissues and organs that produce, store, and carry white blood cells) and the lymph nodes.

SYMPTOMS AND DIAGNOSIS

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

Diagnosis of MCL requires careful evaluation of the cancer cells, frequently by lymph node biopsy (removing a piece of the affected lymph node) and looking at the cells under a microscope. Other tests that can be helpful include the following:

- Testing for cancer cells in the bloodstream
- A bone marrow biopsy (removal of a small piece of the bone marrow) or an endoscopy (a procedure to examine the upper part of the digestive system) to look for lymphoma that is not detected on scans
- Imaging with a computed tomography (CT) scan or positron emission tomography (PET) scan. These tests help monitor disease progression (how the cancer grows and spreads). PET scans use a special dye that accumulates in places where the cancer is located

Specific testing that can be helpful includes the following:

- Excessive amounts of a protein called cyclin D1 (found in > 90% of patients with MCL)
- A genetic mutation (permanent change) in the DNA (deoxyribonucleic acid, the molecule that carries the genetic information) named t(11;14)(q13;q32) translocation (Figure 2). This translocation is the reason behind the abnormal presence of the cyclin D1 protein

- High levels of Ki-67, a protein associated with cell multiplication in MCL that multiplies quickly
- High levels of an abnormal p53 protein (due to a mutation in the TP53 gene) or loss of the TP53 gene. A gene is a small piece of DNA that contains information for making specific proteins
- Excessive levels of lactate dehydrogenase (LDH), which is usually present in larger tumors that grow rapidly

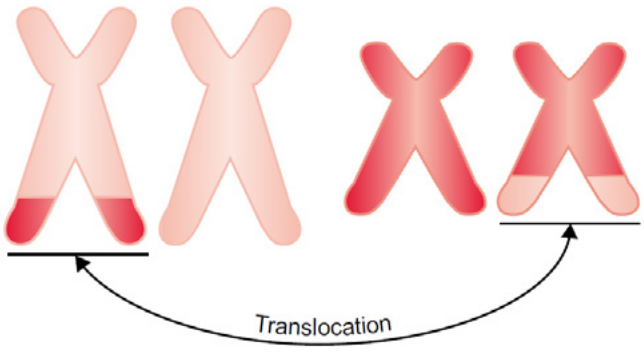

Figure 2. The t(11;14)(q13;q32) translocation, where a chromosome (a structure made of DNA and proteins found inside the cell) breaks, and part of it reattaches to another chromosome.

Measuring these and other markers can help physicians determine how aggressive the MCL is and may guide therapy decisions.

TREATMENT OPTIONS

The type of treatment selected for a patient with MCL depends on multiple factors, including:

- How fast the cancer is growing
- Problems with the TP53 gene
- The patient's overall health

For the patients who do not yet have symptoms and who have a limited amount of slow-growing disease, monitoring through observation may occur with no treatment given. This approach is called active surveillance, also known as watchful waiting. In this case, patients' overall health and disease are monitored through regular checkup visits that may include physical examination (like checks for any swelling) and other tests (like bloodwork and imaging scans). Treatment is started if the patient begins to develop MCL-related symptoms, or there are signs that the disease is progressing (growing). MCL is usually diagnosed once it has spread throughout the body, and the majority of patients, ultimately, will require treatment.

Initial treatment approaches for MCL can vary significantly and can change when new treatment information becomes available. A common option in younger patients is the combination of a monoclonal antibody (a protein made in a laboratory that binds to markers at the surface of cancer cells and helps the body fight cancer), rituximab (Rituxan), and a cytarabine (Cytosar), which contains combination chemotherapy regimen. This is often followed by an autologous stem cell transplantation (patient's own cells are infused after high-dose chemotherapy). This treatment may be followed by an extended course (prolonged treatment) of a rituximab product, known as maintenance therapy. This can be done with rituximab (Rituxan) or a rituximab biosimilar (a molecule made inside a living cell that is modeled after rituximab). The goal is to achieve durable remission (no signs of cancer for a long period of time).

Patients who are older or less fit can receive other types of frontline (initial) therapy, like less-intensive (lower dose) chemotherapy, with or without rituximab (Rituxan). An example is the BR regimen, which consists of bendamustine (Treanda) in combination with rituximab (Rituxan). A recent trial supported the use of the Bruton tyrosine kinase (BTK; a protein that lymphoma cells use to grow) inhibitor ibrutinib (Imbruvica), in addition to BR.

Bortezomib (Velcade) is approved by the U.S. Food and Drug Administration (FDA) for the treatment of patients with MCL. Studies with bortezomib (Velcade) show that the drug may be effectively combined with rituximab (Rituxan) and prednisone, plus the chemotherapy drugs cyclophosphamide and doxorubicin (adriamycin) (VR-CAP). This combination is known as VR-CAP.

For patients whose disease has relapsed (returned after treatment) or became refractory (didn't respond to treatment), other therapeutic options are available, such as zanubrutinib (Brukinsa), acalabrutinib (Calquence), and pirtobrutinib (Jaypirca). These BTK inhibitors stop signals in cancer cells responsible for growth and survival. Other therapeutic options for relapsed or refractory MCL include:

- Lenalidomide (Revlimid, an immunomodulatory drug [a drug that works on the immune system directly by regulating specific proteins])
- Brexucabtagene autoleucel (Tecartus, a chimeric antigen receptor [CAR] T-cell therapy)
- Allogeneic stem cell transplantation (patients receive stem cells from a familiar or unrelated donor)

For more information on relapsed or refractory disease, view our *Mantle Cell Lymphoma: Relapsed/Refractory* fact sheet (visit **lymphoma.org/publications**). Patients seeking more information about stem cell transplantation and/or CAR T-cell therapy should view the *Understanding Cellular Therapy* guide on Lymphoma Research Foundation (LRF)'s website (**lymphoma.org/publications**).

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 LRF for any treatment updates that may have recently appeared.

TREATMENTS UNDER INVESTIGATION

Many new treatments (also referred to as investigational drugs) are being studied in clinical trials for patients with newly diagnosed MCL. These include attempts to determine who most benefits from stem cell transplantation and the use of new drugs to replace or shorten the course of chemotherapy. Other important trials include combinations of BTK inhibitors and other targeted drugs. 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). For more information on clinical trials, view the *Understanding Clinical Trials* fact sheet on the

LRF website at **lymphoma.org/publication**. Below are some of the investigational drugs that can be accessed through a clinical trial:

- Venetoclax (Venclexta)
- Obinutuzumab (Gazyva)
- Orelabrutinib
- Palbociclib (Ibrance)
- Copanlisib (Aliqopa)
- Ixazomib (Ninlaro)
- Zilovertamab
- Zilovertamab vedotin

Please view the *Mantle Cell Lymphoma: Relapsed/Refractory* fact sheet (visit **lymphoma.org/publications**) for information about treatments being evaluated for relapsed/refractory MCL.

CLINICAL TRIALS

Clinical trials are crucial in identifying effective drugs and optimal treatment doses for patients with lymphoma. Because the optimal initial treatment of MCL is not clear, and it is such a rare disease, clinical trials are very important to identify the best treatment options for this disease. Patients interested in participating in a clinical trial should view the *Understanding Clinical Trials* fact sheet on LRF's website (visit **lymphoma.org/publications**), 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 relapsed or refractory MCL should have regular visits with their physician. During these visits, medical tests (such as blood tests, CT scans, and 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 a 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 can vary depending on the following factors:

- Duration of treatment (how long the treatment lasted)
- Frequency of treatment (how often the treatment was administered)
- Type of treatment given
- Age and gender of the patient
- Patient's overall health at the time of treatment

A physician will check for these effects during follow-up care. Visits may become less frequent the longer the patient stays in remission.

Patients and their caregivers are encouraged to keep copies of all medical records. This includes test results, as well as information on the type, amount, and duration of all treatments received. Medical records 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 can help patients manage this documentation.

LYMPHOMA CARE PLAN AND PATIENT EDUCATION PROGRAMS

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. LRF's *Lymphoma Care Plan* fact sheet 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* fact sheet can be accessed by visiting **lymphoma.org/publications**. LRF also offers a variety of educational activities, including live meetings and webinars, for individuals looking to learn directly from lymphoma experts. To view our schedule of upcoming programs, please visit **lymphoma.org/programs**.

LRF Helpline

The LRF 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. LRF 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 LRF 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**).

LRF FOCUS ON LYMPHOMA MOBILE APP

Focus on Lymphoma is the first app to provide patients and their caregivers with tailored content based on lymphoma subtype and actionable tools to better manage diagnosis and treatment. It provides convenient and comprehensive lymphoma management 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 LRF Helpline at **800-500-9976** or **helpline@lymphoma.org**.

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