Understanding Lymphoma and Chronic Lymphocytic Leukemia (CLL)

Mantle Cell Lymphoma

Lymphoma Research Foundation

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 the 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 esophagus, stomach, and intestines), bone marrow (the spongy tissue inside the bone), bloodstream, and other sites at the time of diagnosis.

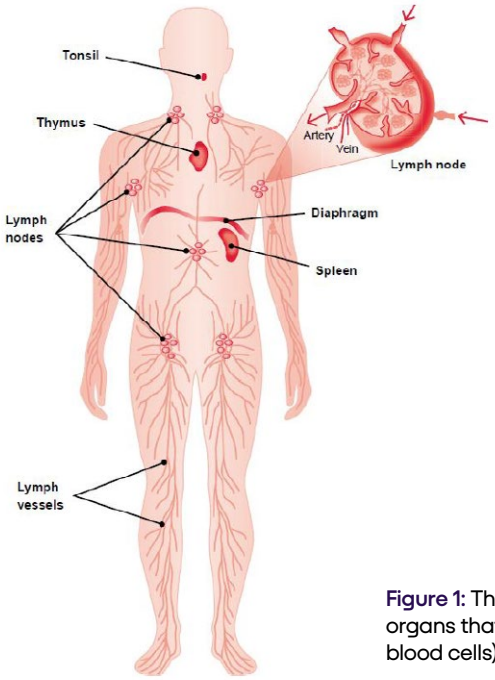

Figure 1: The lymphatic system (tissues and organs that produce, store, and carry white blood cells) and lymph nodes.

Symptoms and Diagnosis

Some patients with MCL do not have any symptoms. Other patients may develop a 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* (removing 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/CT (PET/CT) scan. These tests help monitor disease progression (how the cancer grows and spreads). PET scans use a special dye that accumulates inside cancer cells and lets the doctors know where the cancer is.

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 Ki67, a protein associated with cell multiplication (in MCL that multiply 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 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.

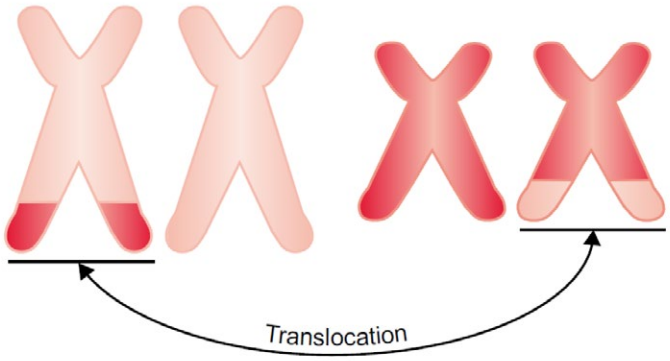

Figure 2: The t(11;14)(q13;q32) translocation, where a *chromosome* (a structure made of DNA and proteins found inside the cell) breaks and part of it reattaches to another chromosome.

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, patients might be monitored through observation 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 checking 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 will ultimately require treatment.

Initial treatment approaches for MCL can vary significantly and can change when new treatment information becomes available. Types of initial treatment for MCL can include:

- Chemoimmunotherapy, a combination of chemotherapy (drugs that stop the growth of or kill cancer cells) with immunotherapy (drugs that use the body's immune system to fight cancer)
- Immunotherapy, including:
  - Monoclonal antibodies (a protein made in the laboratory that binds to markers at the surface of cancer cells and helps the body fight cancer)
- 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)
- Targeted therapy, drugs that target specific molecules that cancer cells use to survive and spread.

A common option in younger patients is the combination of the monoclonal antibody, rituximab (Rituxan), with a cytarabine (Cytosar)-containing combination chemotherapy regimen. In some cases, this may be followed by an *autologous* SCT (patient's own stem 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). New data suggest that the addition of Bruton tyrosine kinase (BTK) inhibitors (a type of targeted therapy) may be beneficial.

Patients who are older or less fit can receive other type of *frontline* (initial) therapy, like less-intensive (using lower doses) chemotherapy with or without rituximab (Rituxan). An example is the BR regimen, which consists of bendamustine (Treanda) in combination with rituximab (Rituxan). Some patients may benefit from maintenance therapy (additional treatment after the cancer has responded to initial treatment) with rituximab (Rituxan) and/or a BTK inhibitor.

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, prednisone plus the chemotherapy drugs cyclophosphamide and adriamycin (VR-CAP).

For patients whose lymphoma has *relapsed* (returned after treatment) or became *refractory* (does not respond to treatment), other therapeutic options are available,

- Combination chemotherapy regimens with monoclonal antibodies
- Targeted therapies such as zanubrutinib (Brukinsa), acalabrutinib (Calquence), and pirtobrutinib (Jaypirco). These drugs are called Bruton tyrosine kinase (BTK) inhibitors and stop signals in cancer cells responsible for growth and survival.
- Targeted therapy with the immunomodulatory drug lenalidomide (Revlimid)
- Targeted therapy with bortezomib (Velcade).
- Chimeric antigen receptor (CAR) T cell therapy, a special form of immunotherapy that uses the patient's own immune cells to fight cancer such as brexucabtagene autoleucel (Tecartus)
- Allogeneic SCT (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* factsheet (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 the Foundation'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 Lymphoma Research Foundation 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. Several trials include attempts to use new drugs to replace or shorten the course of chemotherapy, including stem cell transplantation. In most cases, these trials include drugs that are already commonly used for previously treated 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). For more information on clinical trials, view the *Understanding Clinical Trials* publication on the Lymphoma Research Foundation's website at **lymphoma.org/publication**.

Please view the *Mantle Cell Lymphoma: Relapsed/Refractory* factsheet (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* 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 lymphoma 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.

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 effects can vary based 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 effects during follow-up care. Visits may become less frequent the longer the patient stays in remission.

Patients and their care partners are encouraged to keep copies of all medical records. This includes test results, as well as information on the types, amounts, 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. The Foundation's award-winning *Focus On Lymphoma* mobile app 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**.

Lymphoma Research Foundation

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Helpline
(800) 500-9976
helpline@lymphoma.org

lymphoma.org
lymphoma@lymphoma.org

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