LYMPHOMA RESEARCH • FOUNDATION

Understanding Mantle Cell Lymphoma

Mantle cell lymphoma (MCL) is a rare B-cell non-Hodgkin lymphoma (NHL). Although it is more common in men over the age of 60, it can affect men and women of all ages.

Mantle cell lymphoma (MCL) is a rare B-cell non-Hodgkin lymphoma (NHL). Although it is more common in men over the age of 60, it can affect men and women of all ages. The disease often starts out in a more *indolent* (slow-growing) manner but can become more *aggressive* (fast-growing) over time. MCL comprises about five percent of all NHLs. The disease is called "mantle cell lymphoma" because the tumor cells originally come from the "mantle zone" of the lymph node. MCL is usually diagnosed as a late-stage disease and is often present in the gastrointestinal tract, bone marrow, bloodstream, and other non-lymph node sites.

A diagnosis of MCL requires taking a sample of tumor tissue, called a biopsy, and looking at the cells under a microscope. Other tests of the lymphoma cells are necessary to verify a diagnosis of MCL and distinguish it from other subtypes of NHL, including routinely used panels of lymphocyte (immune cell) markers. Imaging with a computed tomography (CT) scan or positron emission tomography/CT (PET/CT) scan is routinely used to determine what areas of the body are involved by the cancer. Occasionally, a bone marrow biopsy or endoscopy is performed to help identify lymphoma that might not be evident on scans.

Overproduction of a protein called cyclin D1 in the lymphoma cells is found in more than 90 percent of patients with MCL. Identification of excess cyclin D1 from a biopsy, as well as a characteristic genetic mutation referred to as t(11;14) (q13;q32) translocation, are considered very sensitive tools for diagnosing MCL and providing prognostic information. Testing for a protein called Ki67 (which increases when cells are preparing to divide) in tumor tissue from lymph nodes can provide clinicians with an idea about the proportion of lymphoma cells that are actively dividing. Abnormalities in the TP53 gene (which makes the p53 protein, the gatekeeper of cell division), can be associated with reduced responsiveness to some treatments. One-quarter to one-half of patients with MCL also have higher-than-normal levels of certain proteins that circulate in the blood, such as lactate dehydrogenase (LDH) and beta-2 microglobulin.

Measuring these and other markers can help physicians determine how aggressive an individual patient's MCL is and may guide therapy decisions.

TREATMENT OPTIONS

The type of treatment selected for a patient with MCL depends on multiple factors, including the stage of disease, the age of the patient, and the patient's overall health. For the subset of patients who do not yet have symptoms and who have a relatively small volume of slow-growing disease, *active surveillance*, also known as *watchful waiting* (observation with no treatment [drug therapy, radiation therapy, or stem cell transplantation] given) may be an acceptable option. With this strategy, patients' overall health and disease are monitored through regular checkup visits and various evaluation procedures, such as physical examination and laboratory or imaging tests. Active treatment is started if the patient begins to develop MCL-related symptoms or there are signs that the disease is progressing. 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 in younger patients include the monoclonal antibody, rituximab (Rituxan), with a cytarabine (Cytosar)-containing combination chemotherapy regimen, and are often followed by consolidation with *autologous stem cell transplantation* (patient's own cells are infused after high-dose chemotherapy). This treatment may be followed by an extended course of rituximab (Rituxan) alone, known as maintenance therapy, with the goal of prolonging *remissions* (disappearance of signs and symptoms). For older or less fit patients, less-intensive chemotherapy is often

recommended and may also be followed by rituximab (Rituxan) maintenance. One such treatment is bendamustine (Treanda) in combination with rituximab (BR) as a *frontline* (initial) therapy.

Zanubrutinib (Brukinsa) and acalabrutinib (Calquence) are Bruton tyrosine kinase (BTK) inhibitors that stop signals in cancer cells responsible for growth and survival. Both are approved by the FDA for treatment of MCL in patients who have received at least one prior therapy. Brexucabtagene autoleucel [Tecartus, a chimeric antigen receptor (CAR) T cell therapy] is also approved in patients who have received at least one prior therapy, but it is most commonly used in patients who have received a prior BTK inhibitor.

Other therapeutic options available for patients whose disease has relapsed (returned after treatment) or became refractory (does not respond to treatment) include lenalidomide (Revlimid, an immunomodulatory drug that is commonly combined with rituximab) and bortezomib (Velcade). Jaypirca is a kinase inhibitor indicated for the treatment of adult patients with relapsed or refractory mantle cell lymphoma (MCL) after at least two lines of systemic therapy, including a BTK inhibitor.

Allogeneic stem cell transplantation (patients receive stem cells from a familiar or unrelated donor) is also a treatment option. For more information on relapsed or refractory disease, view our *Mantle Cell Lymphoma: Relapsed/Refractory* factsheet (click **here**).

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.

TREATMENTS UNDER INVESTIGATION

Many new approaches are being studied as initial therapy in clinical trials for 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.

New agents being investigated alone or as a part of combination therapy for newly diagnosed MCL include the following:

- Venetoclax (Venclexta)
- Obinutuzumab (Gazyva)
- Pirtobrutinib
- Palbociclib (Ibrance)
- Copanlisib (Aliqopa)
- Ixazomib (Ninlaro)

Please view the *Mantle Cell Lymphoma: Relapsed/Refractory* factsheet (click **here**) for information about treatments being evaluated for relapsed/refractory MCL.

CLINICAL TRIALS

Clinical trials are crucial in identifying effective drugs and determining optimal 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 in this disease. Patients interested in participating in a clinical trial should view the *Understanding Clinical Trials* factsheet on LRF's website (click here), 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, CT scans, and 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 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 effects during follow-up care.

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 HELPLINE AND LYMPHOMA SUPPORT NETWORK

A lymphoma diagnosis often triggers a range of feelings and concerns. In addition, cancer treatment can cause physical discomfort. The LRF Helpline staff members are available to answer your general questions about a lymphoma diagnosis 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. A part of the Helpline is LRF's one-to-one peer support programs, Lymphoma Support Network. This program connects patients and caregivers with volunteers who have experience with MCL, similar treatments, or challenges, for mutual emotional support and encouragement. Patients and loved ones may find this useful whether the patient is newly diagnosed, in treatment, or in remission.

MOBILE APP

Focus On Lymphoma is the first mobile application (app) that provides patients and caregivers comprehensive content based on their lymphoma subtype, including MCL, and tools to help manage their lymphoma such as, keep track of medications and blood work, track symptoms, and document treatment side effects. The *Focus On Lymphoma* mobile app is available for download for iOS and Android devices in the Apple App Store and Google Play. For additional information on the mobile app, visit FocusOnLymphoma.org. To learn more about any of these resources, visit our website at lymphoma.org, or contact the LRF Helpline at 800-500-9976 or helpline@lymphoma.org.

Resources

LRF offers a wide range of free resources that address treatment options, the latest research advances, and ways to cope with all aspects of lymphoma and MCL. LRF also provides many educational activities, including our in-person meetings, podcasts, and webinars for people with lymphoma. For more information about any of these resources, visit our websites at lymphoma.org/MCL or lymphoma.org, or contact the LRF Helpline at (800) 500-9976 or helpline@lymphoma.org.

LRF appreciates the expertise and review of our Editorial Committee:

Leo I. Gordon, MD, FACP
Co-Chair
Robert H. Lurie Comprehensive Cancer Center of Northwestern University

Kristie A. Blum, MD
Co-Chair
Emory University School of Medicine

John Allan
Weill Cornell Medicine

Jennifer E. Amengual, MD
Columbia University

Jonathon Cohen
Emory University School of Medicine

Alex Herrera, MD
City of Hope

Shana Jacobs, MD
Children's National Hospital

Manali Kamdar, MD
University of Colorado

Peter Martin, MD,
Weill Cornell Medicine

Anthony Mato, MD
Memorial Sloan Kettering Cancer Center

Neha Mehta-Shah, MD, MSCI
Washington University School of Medicine in St. Louis

Pierluigi Porcu, MD
Thomas Jefferson University

Contact LRF:

Helpline: (800) 500-9976

Email: helpline@lymphoma.org

www.lymphoma.org

Supported through grants from: Bristol Myers Squibb, Genentech | Biogen, pharmacyclics, Kite, BeiGene

Last updated 2022

Stay Connected through our social media: