

Mantle Cell Lymphoma: Relapsed/Refractory

Overview

Lymphoma is the most common blood cancer. The two main forms of lymphoma are Hodgkin lymphoma and non-Hodgkin lymphoma (NHL). Lymphoma occurs when cells of the immune system called lymphocytes, a type of white blood cell, grow and multiply uncontrollably. Cancerous lymphocytes can travel to many parts of the body, including the lymph nodes, spleen, bone marrow, blood, or other organs, and form a mass called a tumor. The body has two main types of lymphocytes that can develop into lymphomas: B lymphocytes (B cells) and T lymphocytes (T cells).

Mantle cell lymphoma (MCL) is a rare type of B-cell NHL that may be either *aggressive* (fast-growing) or *indolent* (slow-growing). It most often affects men over the age of 60. 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 at an advanced stage when it may have already spread to the spleen and lymph nodes as well as the gastrointestinal tract and bone marrow.

Although MCL usually responds well to initial treatment, patients often *relapse* (disease returns after treatment) within a few years. For patients who relapse or become *refractory* (disease does not respond to treatment), secondary therapies may be successful in providing another *remission* (disappearance of signs and symptoms).

Treatment Options

Like other forms of NHL, there is no consensus on the best treatment for relapsed or refractory MCL; however, there are an increasing number of treatment options. The type of treatment recommended for any individual patient depends on several factors, including the timing of the relapse, the patient’s age, extent of disease, overall health, and prior therapies received.

Four agents have been approved by the U.S. Food and Drug Administration (FDA) for treatment of relapsed or refractory MCL:

- Acalabrutinib (Calquence)
- Bortezomib (Velcade)
- Ibrutinib (Imbruvica)
- Lenalidomide (Revlimid)

Although not approved in combination, any of the previously mentioned drugs may be used with rituximab (Rituxan). Additional agents and regimens that are commonly used for the treatment of relapsed/refractory MCL include:

- Bendamustine (Treanda) with or without rituximab (Rituxan)
- Combination chemotherapy with or without rituximab (Rituxan)

Stem cell transplant (SCT) can be effective in patients with relapsed or refractory MCL. There are two types of SCTs: *allogeneic* (patients receive stem cells from another person) and *autologous* (patients receive their own stem cells). Autologous SCT is generally considered after initial therapy rather than in relapse, but may be an option for medically fit patients who have shown a good response to later therapies. In the case of younger, medically fit patients, intensive chemotherapy followed by allogeneic stem cell transplantation is a higher risk, but potentially a curative option. For more information on transplantation, view the *Understanding the Stem Cell Transplantation Process* publication on the Lymphoma Research Foundation’s (LRF’s) website at lymphoma.org/publications.

Treatments Under Investigation

There are several clinical trials investigating the effectiveness of various new agents to be used in combination with current or new combination therapies for relapsed or refractory MCL including:

- Acalabrutinib (Calquence)
- ADCT-402
- Alisertib
- Belinostat (Beleodaq)
- Blinatumomab (Blincyto)
- Buparlisib
- Camidanlumab tesirine
- Carfilzomib (Kyprolis)
- Daratumumab (Darzalex)
- Duvortuxizumab
- Entospletinib
- Enzalutamide (Xtandi)
- Everolimus (Afinitor)
- Ibritumomab tiuxetan (Zevalin)
- Idelalisib (Zydelig)
- Ixazomib (Ninlaro)
- Nivolumab (Opdivo)
- Obinutuzumab (Gazyva)
- Onalespib
- Palbociclib (Ibrance)
- Pembrolizumab (Keytruda)
- Ramucirumab (Cyramza)
- Romidepsin (Istodax)
- SS55746/BCL201
- Temsirolimus (Torisel)
- Umbralisib
- Venetoclax (Venclexta)

Additionally, novel combinations of agents currently used in MCL as well as genetically engineered T cells designed to recognize and kill MCL cells, referred to as chimeric antigen receptor (CAR) T-cell therapy, such as axicabtagene ciloleucel (Yescarta) and tisagenlecleucel (Kymriah) are also being studied.

Treatment options are changing as new therapeutics are becoming available and current treatments are improved. Because today's scientific research is continuously evolving, it is important that patients check with their physician or with 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. Because the optimal initial treatment of MCL is not clear and it is such a rare disease, clinical trials are very important and will 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 at 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 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 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.

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 mobile app *Focus On Lymphoma* (lymphoma.org/mobileapp) and the *Lymphoma Care Plan* (lymphoma.org/publications) 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. One-to-one peer support programs, such as LRF's *Lymphoma Support Network*, connect patient and caregivers with volunteers who have experience with lymphoma or 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.

Resources

LRF offers a wide range of resources that address treatment options, the latest research advances, and ways to cope with all aspects of lymphoma and MCL, including our award-winning mobile app.

LRF also provides many educational activities, from in-person meetings to teleconferences and webcasts for people with lymphoma and MCL, as well as patient guides and e-Updates that provide the latest disease-specific news and treatment options. 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.

Contact the
Lymphoma Research Foundation

Helpline: (800) 500-9976

helpline@lymphoma.org

Website: lymphoma.org

Medical reviewer:

Peter Martin, MD

Weill Cornell Medicine

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