

Understanding Mantle Cell Lymphoma: Relapsed/Refractory

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.

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 node. By the time a person is diagnosed, MCL is usually present throughout the body, in the lymph nodes, spleen, bone marrow, and gastrointestinal tract.

Although patients may not need treatment at the time of diagnosis, MCL usually reacts well to the first treatment. The amount and period of time of the *remission* (disappearance of signs and symptoms) may be different because of things like lymphoma biology and the kind of treatment given. Most patients will need treatment more than one time.



TREATMENT OPTIONS

There are a number of treatment options for the management of *relapsed/refractory* (returns after or no longer responds to treatment) MCL, and the number of treatment choices is going up. The type of treatment recommended depends on several things, including what treatments were already given, when the relapse took place, and the patient’s age and overall health.

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

- Acalabrutinib (Calquence)
- Bortezomib (Velcade)
- Brexucabtagene Autoleucl (Tecartus)
- Ibrutinib (Imbruvica)
- Lenalidomide (Revlimid)
- Zanubrutinib (Brukinsa)

Although they are not approved to be given together, any of the drugs mentioned above may be used with rituximab (Rituxan) or rituximab biosimilars. Biosimilars are drugs that are modeled after a biologic therapy that already exists. Biosimilars include rituximab-abbs and rituximab-pvvr. To learn more, please see the *Biosimilars* factsheet on the Lymphoma Research Foundation’s (LRF’s) website at Lymphoma.org/publications. Additional drugs and combinations of drugs 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 work well in patients with relapsed or refractory MCL. There are two types of SCTs: *autologous* (a patient’s own cells are put back into the patient after high-dose chemotherapy) and *allogeneic* (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, but SCT may have more risks. For more information on transplantation, see the *Understanding the Stem Cell Transplantation Process* publication at lymphoma.org/publications.



TREATMENTS UNDER INVESTIGATION

There are several clinical trials investigating how safe and effective these new drugs are, either used alone or together with current or new therapies, for MCL that has already been treated. These include:

- ARQ 531
- Camidanlumab tesirine
- Carfilzomib (Kyprolis)
- Cirmtuzumab and VLS-101
- Aliqopa (Copanlisib)
- Enzalutamide (Xtandi)
- Everolimus (Afinitor)
- DTRMWXHS-12
- Parsaclisib
- Ixazomib (Ninlaro)
- Loncastuximab tesirine
- LOXO-305
- Mosunetuzumab
- Nivolumab (Opdivo)
- Obinutuzumab (Gazyva)
- ONC201

- Orelabrutinib
- Palbociclib (Ibrance)
- Pembrolizumab (Keytruda)
- PRT543
- REGN1979
- Temsirolimus (Torisel)
- Umbralisib
- Vecabrutinib
- Venetoclax (Venclexta)

Genetically engineered T cells, which are designed to recognize and kill MCL cells, are also being studied to treat MCL. This type of treatment is known as chimeric antigen receptor (CAR) T-cell therapy, and it includes drugs such as axicabtagene ciloleucel (Yescarta), lisocabtagene maraleucel, JCAR017, JCAR018, and tisagenlecleucel (Kymriah), and others. To learn more, please refer to the *CAR T-Cell Therapy* factsheet at lymphoma.org/publications.

Treatment choices are increasing as new drugs are developed and current treatments are improved. Because the science is always changing, it is important for patients to check in with their doctor or with LRF to find out about any new treatments that become available.

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 enrollment is critical for establishing more effective, 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 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

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during remission to evaluate the need for additional treatment. Periodically, it may be necessary to repeat a tumor biopsy to better understand the biology of the lymphoma.

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. Visits may become less frequent the longer the disease remains in remission.

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 *Focus On Lymphoma mobile app* (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, webinars for people with lymphoma and MCL, as well as patient guides and e-Updates that provide the latest disease-specific news and treatment options. To learn more 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.

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