

## 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.

### 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 available for these patients. 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.

Several therapeutics are currently used as single agents or as part of a combination therapy regimen:

- Bendamustine (Treanda) ± rituximab
- Bortezomib (Velcade) ± rituximab
- Ibrutinib (Imbruvica)

- Lenalidomide (Revlimid) ± rituximab
- Radioimmunotherapy (<sup>90</sup>Y-ibritumomab tiuxetan; Zevalin)

Stem cell transplant (SCT) can be effective in patients with relapsed or refractory MCL. There are two types of SCTs: allogeneic (in which patients receive stem cells from another person) and autologous (in which 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 treatment of their relapsed MCL. 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.

### 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:

- Carfilzomib (Kyprolis)
- Everolimus (Afinitor)
- Ibritumomab tiuxetan (Zevalin) combination therapies
- Ibrutinib (Imbruvica) combination therapies
- Idelalisib (Zydelig)
- Lenalidomide combination therapies
- Panobinostat (Farydak)
- PEPC (prednisone, etoposide, procarbazine, cyclophosphamide) ± rituximab or thalidomide
- Romidepsin (Istodax)
- Temsirolimus (Torisel)
- Venetoclax (ABT-199; BCL2 inhibitor)
- Vorinostat (Zolinza)

Some agents (e.g., bendamustine, lenalidomide, rituximab) are being tested together as a combination regimen or are being tested in combination with chemotherapy agents such as bortezomib, ibrutinib, and temsirolimus. Others are being assessed in head-to-

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head trials (ibrutinib vs. temsirolimus) to determine new treatment approaches. 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 the Lymphoma Research Foundation (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* fact sheet on LRF's website at [www.lymphoma.org](http://www.lymphoma.org), 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](mailto:helpline@lymphoma.org).

## Follow-up

Patients in remission 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 and computed axial tomography [CAT] scans) may be required at various times during remission to evaluate the need for additional treatment.

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 effects resulting from treatment or potential disease recurrences.

## Support

A lymphoma diagnosis often triggers a range of feelings and raises concerns. In addition, cancer treatment can cause physical and emotional discomfort. Support groups and online message boards can help patients connect with other people who have lymphoma. One-to-one peer support programs, such as the LRF Lymphoma Support Network, match lymphoma patients (or caregivers) with volunteers who have gone through similar experiences.

## 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, including our award-winning mobile app. LRF also provides many educational activities, from in-person meetings to teleconferences and webcasts, as well as disease-specific websites, videos, and eNewsletters for current lymphoma information and treatment options. To learn more about any of these resources, visit our websites at [www.FocusOnMCL.org](http://www.FocusOnMCL.org) or [www.lymphoma.org](http://www.lymphoma.org), or contact the LRF Helpline at (800) 500-9976 or [helpline@lymphoma.org](mailto:helpline@lymphoma.org).