

Mantle Cell Lymphoma (MCL)



OVERVIEW

Lymphoma is the 6th most common cancer in Australia in adult men and women. It can affect people of all ages and is the most common blood cancer. Lymphoma is a cancer of the immune system and affects lymphocytes - a type of white blood cell. When lymphocytes gain DNA mutations they divide and grow uncontrollably resulting in lymphoma.

There are two main types of lymphocytes - B-cells and T-cells. Lymphomas growing from B-cells are more common and account for around 85% of lymphoma cases; those caused by T-cells around 15%. The first lymphoma to be discovered was 'Hodgkin lymphoma' (HL - around 15% of all B-cell lymphomas), after Thomas Hodgkin, who described it. All subsequent lymphomas discovered were called 'non-Hodgkin lymphoma' (NHL - around 90% of all lymphomas, both B and T-cell lymphomas).

There are over 80 different subtypes of lymphoma, which can be classified according to how fast they grow. 'Aggressive' (or high-grade) lymphomas are those that grow quickly, usually weeks to months and need treatment immediately. 'Indolent' (or low-grade) lymphomas usually develop over months to years and often are not treated straight away but are monitored. It is important to know your subtype of lymphoma. Lymphoma cells can travel to any part of the body and be found in lymph nodes, the bone marrow, the spleen, blood, bone, skin and almost any organ or tissue.

Mantle cell lymphoma (MCL) is a rare subtype of B-cell lymphoma that affects men more than women, usually in patients over 60. MCL accounts for 5-10 percent of all NHLs. The disease is called 'mantle cell lymphoma' because the lymphoma cells grow from the 'mantle zone' (the outer edge) of the lymph node. About 85% of people with MCL have a characteristic genetic change in the B-cells where two chromosomes, 11 and 14 break apart to then join together with each other. This is called 'translocation' and causes the cells to produce too much of a protein called cyclin D1. In normal quantities, cyclin D1 helps to promote normal cell growth, however excess amounts result in uncontrolled growth of mantle zone cells which can lead to MCL.

MCL may be aggressive (fast growing), but in a small proportion of patients it can also behave in a more indolent (slow growing)

fashion. Indolent MCL often have circulating MCL cells in the blood and an enlarged spleen without enlarged lymph nodes. Usually the first sign of MCL is a painless swelling in the neck, armpit and/or the groin. Multiple lymph nodes may be affected, as well as other sites of the body including the spleen, the bone marrow, blood, tonsils, lungs, liver, brain/spinal cord and gut. MCL in the gut can result in diarrhea, blood in the stools or iron deficiency. Other symptoms may include abdominal bloating, nausea, tiredness, loss of appetite, fevers, unexplained weight loss and night sweats.

DIAGNOSIS AND STAGING

A biopsy is always required for a diagnosis of MCL. A biopsy is a surgical procedure to remove part of or all of an affected lymph node or other abnormal tissue to look at it under the microscope. The biopsy can be done under local or general anaesthetic depending on what part of the body is being biopsied.

Once a diagnosis of MCL is made there are further tests that need to be performed to see where else in the body the lymphoma may be and is referred as staging. Because MCL is a blood cancer the lymphoma can travel all over the body, so it is important that a check of the entire body is done looking for the lymphoma. The majority of patients with MCL have stage IV disease at diagnosis. Staging tests may include:

- Positron emission tomography (PET) /CT scan
- Computed tomography (CT) scan
- Bone marrow biopsy
- Lumbar puncture (if lymphoma suspected in the brain or spinal cord)
- Baseline tests prior to any treatment commencing to check their organ function that may include a heart scan, kidney scan, and blood tests

TREATMENT OPTIONS

The type of treatment selected for a person with MCL depends on many factors, including the stage of disease, the symptoms present, the age of the person and their overall health. For people who have indolent MCL with no symptoms the treatment is often 'watch and wait' (see fact sheet 'Understanding Watch & Wait') where the person is monitored until they have symptoms or the MCL has progressed.

FACT SHEET

For those with aggressive MCL, treatment is usually required straight away. The choice of treatment depends on the individual patient and their fitness. Common treatment protocols include:

- R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine and prednisolone)
- R-DHAP (dexamethasone, cisplatin and cytarabine) +/- alternating cycles with R-CHOP
- R-maxi CHOP with alternating cycles of rituximab and cytarabine (aka Nordic MCL2 protocol)
- Hyper-CVAD (Part A: cyclophosphamide, doxorubicin, vincristine +/- alternating cycles with Part B: methotrexate & cytarabine)
- autologous stem cell transplant, considered for fitter patients aged <70 after first line treatment for consolidation
- Bendamustine and rituximab
- Patients with stage I-II MCL may receive radiotherapy +/- chemotherapy

Treatment is often successful initially in many patients with MCL, however relapses are common. When MCL comes back (relapses) and further treatment is needed, treatment options include:

- Clinical trial
- Ibrutinib (Imbruvica™ a BTK inhibitor)
- Lenalidomide (Revlimid™)
- Combination chemotherapy
- A select few younger, and fitter patients may be considered for allogeneic stem cell transplantation

TREATMENTS UNDER INVESTIGATION

Many new individual and combination medicines are currently being tested in clinical trials around the world for both newly diagnosed, relapsed and refractory MCL including:

- Venetoclax (Venclexta™)
- Zanubrutinib (Brukinsa™)
- Acalabrutinib (Calquence™)
- Bispecific antibody (eg. mosunetuzumab)
- Obintuzumab (Gazyva™)
- Umbralisib (PI3K inhibitor)
- Bortezomib (Velcade™)
- Chimeric Antigen Receptor (CAR) T-cell Therapy

CLINICAL TRIALS

Clinical trials are essential in identifying effective medicines and determining optimal doses of these medicines for people diagnosed with lymphoma. People who are interested in participating in a clinical trial can find one using the following methods:

1. Speak to their specialist to see what options are available
2. See 'Understanding Clinical Trials' fact sheet for websites to find clinical trials are available; <https://bit.ly/2OFdoKi>

FOLLOW UP

Once treatment is completed, people with lymphoma need to be followed up by their specialist with regular appointments to monitor:

- Evaluate the effectiveness of the treatment
- Ongoing treatment side effects
- Recovery from treatment
- Signs of lymphoma relapsing
- Potential late effects caused by treatment that can occur months or years later, that can be based on the duration and frequency of treatment, age, gender and overall health of each person

RESOURCES AND SUPPORT

Organisation	How can they help?
Lymphoma Australia	<ul style="list-style-type: none">• Please visit our website for more information: lymphoma.org.au• Fact sheets & booklets: lymphoma.org.au/page/1218/fact-sheets• Lymphoma Australia YouTube Channel: Presentations & interviews on various topics including: 'Mantle Cell Lymphoma' youtube.com/user/LymphomaAustralia• Lymphoma Nurse Support Line: 1800 953 081 or email: nurse@lymphoma.org.au• Online private Facebook group: 'Lymphoma Down Under' http://bit.ly/2mrPA1k

SOME QUESTIONS TO ASK YOUR DOCTOR

- Do I have an indolent or aggressive MCL?
- What are the treatment options for my MCL?
- Are there any clinical trials available for me currently?
- If I have an indolent MCL how often will I be followed up?
- Are there any treatment options that are better for my type of lymphoma but are yet to be funded by the PBS in Australia?
- If my MCL has relapsed, will you do another tissue biopsy to confirm this?

This resource was last reviewed and updated February 2020