



"I'm able to stick to my normal routine"



Patients with MCL commonly present with B symptoms^{1,2}



Unexplained fevers
($>100.5^{\circ}\text{F}$)



Unintentional weight loss
($\geq 10\%$ over
6 months or less)



Night sweats

Additional signs and symptoms can include^{1,3,4}



Generalized lymphadenopathy
(70%-80% of cases)



Abdominal distension



Splenomegaly



Hepatomegaly

A small percentage of patients with MCL (much fewer than in CLL) can be asymptomatic and may or may not have lymphocytosis^{1,3,5}

CLL, chronic lymphocytic leukemia; MCL, mantle cell lymphoma.

[REFERENCES >](#)

Asymptomatic disease/
abnormal labs

Symptom onset

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Initial clinical evaluation for patients consists of physical examination, gathering patient history, and conducting laboratory testing¹

Recommended laboratory testing includes^{1,6}



CBC with differential



LDH



Comprehensive metabolic panel



Hepatitis B testing

Bone marrow aspiration and tissue biopsy are conducted following laboratory testing to help establish a diagnosis of MCL, including immunohistochemistry and flow cytometry, as well as histopathologic assessment¹



CBC, complete blood count; LDH, lactate dehydrogenase.

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Once a diagnosis of MCL has been established, imaging (specifically PET-CT or CT) is recommended as part of the staging process to determine the extent of lymph node involvement^{1,6}

MCL staging is typically carried out with Lugano classification criteria, which categorizes lymphoma into 4 stages based on PET-CT imaging^{1,4,7}

Stage I:
1 lymph node region or a single organ

Stage II:
≥2 lymph node regions on the same side of the diaphragm

Stage III:
≥2 lymph node regions above and below the diaphragm

Stage IV:
Widespread disease in lymph nodes and/or other parts of the body

CT, computed tomography; PET, positron emission tomography.
[REFERENCES >](#)



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The MCL International Prognostic Index (MIPI) is one tool used to characterize disease prognosis for patients with MCL^{3,8,9}

- MIPI uses factors such as age, ECOG PS, LDH levels, and WBC count to determine a patient's overall survival prognosis
- MIPI scores used in conjunction with the Ki-67 index can also determine a cumulative prognostic index (biological MIPI)

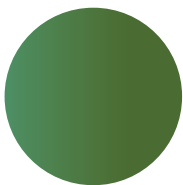
Additionally, prognosis can be determined when the following factors are considered³

- Histological subtype
- Ki-67 positivity
- SOX-11 status
- Complex karyotype
- Somatic mutations (*IGHV*, *TP53*, *ATM*, *NOTCH1/2*)
 - TP53* mutation confers a high-risk, poor-prognostic status, thereby impacting treatment decisions

Genomic and transcriptomic profiling has also helped identify 4 genetic clusters of patients with unique 5-year OS rates¹⁰

Cluster 1

Mutated *IGHV*, *CCND1* mutation, amp(11q), and active BCR signaling



100%

5-year OS rate

Cluster 2

Del(11q)/*ATM* mutations and upregulation of NF-κB and DNA repair pathways

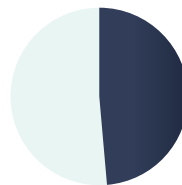


56.7%

5-year OS rate

Cluster 3

Mutations in *SPI40*, *NOTCH1*, and *NSD2*, with downregulation of BCR signaling and MYC targets



48.7%

5-year OS rate

Cluster 4

Del(17p)/*TP53* mutations, del(13q), del(9p), and active MYC pathway and hyperproliferation signatures



14.2%

5-year OS rate

amp(11q), amplification 11q; *ATM*, ataxia-telangiectasia mutated; BCR, B-cell receptor; *CCND1*, cyclin D1; del(9p), deletion 9p; del(11q), deletion 11q; del(13p), deletion 13p; del(17p), deletion 17p; ECOG PS, Eastern Cooperative Oncology Group performance status; *IGHV*, immunoglobulin heavy-chain variable; LDH, lactate dehydrogenase; MYC, myelocytomatosis; NF-κB, nuclear factor kappa B; *NSD2*, nuclear receptor binding SET domain protein 2; OS, overall survival; SOX-11, SRY-box transcription factor 11; *SPI40*, Speckled 140 kDa; *TP53*, tumor protein p53; WBC, white blood cell.

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The majority of patients with MCL will move on to active treatment, whereas some patients have "smoldering" or indolent disease that requires placement into watch and wait status or a clinical trial specific to this early stage of disease^{1,3}



Developing a treatment plan for patients with MCL involves **shared decision-making** between patients and providers after considering stage of disease, risk of progression, overall prognosis, and potential side effects^{11,12}

Effective shared decision-making leverages **SHARE** principles^{12,13}

- S**eek patient participation
- H**elp patients explore and compare treatment options
- A**ssess patient values and preferences
- R**each a decision with the patient
- E**valuate the patient's decision

[REFERENCES >](#)



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The treatment approach to MCL depends on factors including disease stage, transplant eligibility, patient age and fitness, symptom severity, prior treatment history, and other risk factors^{1,14,15}

LOCALIZED DISEASE^{16,17}



Radiotherapy

ADVANCED DISEASE¹⁵⁻²⁰



Chemo-immunotherapy



CAR T-cell therapy



Stem cell transplant



Targeted therapy (including BTKi)

Available advanced disease treatment options by line of therapy¹⁴⁻²²

1L

- Chemoimmunotherapy ± SCT (<65 years of age)
- Chemoimmunotherapy ± steroid therapy (≥65 years of age)
- Covalent BTKi + chemoimmunotherapy

2L

- BTKi naive
 - Covalent BTKi ± chemoimmunotherapy
- BTKi refractory
 - Chemoimmunotherapy
 - Proteasome inhibitor + anti-CD20 antibody

3L+

- BTKi refractory
 - Noncovalent BTKi
 - CAR T-cell therapy

There are limited treatment options for patients who progress after treatment with BTKi²²

1L, first line; 2L, second line; 3L+, third line and beyond; BTKi, Bruton tyrosine kinase inhibitor; CAR, chimeric antigen receptor; CD20, cluster of differentiation 20; SCT, stem cell transplant.

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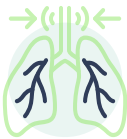
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Each MCL therapy has a unique adverse event profile; however, certain adverse events are common to many treatment types and require timely clinical management and/or prophylaxis



Neutropenia
(5%-49%)^{21,23-26,a}



Upper respiratory tract infection/pneumonia
(10%-39%)^{21,24,26,b}



Anemia
(12%-46%)^{21,23-26,a}



Diarrhea
(19%-39%)^{20,21,23-26,a}



Arthralgia
(8%-37%)^{20,21,24,26,c}



Thrombocytopenia
(16%-44%)^{20,21,23-26,a}



Fatigue
(28%-52%)^{20,21,23,25,26,d}



Nausea
(11%-36%)^{20,21,23,25,26,d}

^aRange based on data from patients with MCL treated with immunotherapy, and targeted therapy (proteasome inhibitors and BTK inhibitors).

^bRange based on data from patients with MCL treated with immunotherapy and targeted therapy (BTK inhibitors).

^cRange based on data from patients with MCL treated with immunotherapy, CAR T-cell therapy, and targeted therapy (BTK inhibitors).

^dRange based on data from patients with MCL treated with immunotherapy, CAR T-cell therapy, and targeted therapy (proteasome inhibitors and BTK inhibitors)

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Patients with MCL typically relapse at some point during their journey, requiring additional treatment in the form of second-line and subsequent therapies, which are chosen based on¹¹



How well previous treatments worked



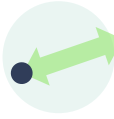
How the patient's MCL has progressed



Whether the patient was tolerant of previous therapies



Patient age and general health



Length of remission

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