

Module 4: Mantle Cell Lymphoma (MCL) Patient Stratification

START

GB: 37205

Date of preparation: July 2022

This non-promotional medical educational resource has been organised and funded by AstraZeneca UK



Tutorial

Glossary terms are identified by bold, yellow text.

Glossary terms are identified by bold, yellow text. Select the word to see the definition

Learning
Objectives

Table of Contents

Glossary

References

Home

Select to close
the pop-up

X

Clinical Connections
encourage connections
between the clinical
content and the patient
journey

Select for more
information

Navigate to the next
or previous page





Module Overview

The MCL Patient stratification module will explain the factors that affect prognosis, as well as the systems used to stratify patients according to risk and stage of MCL progression.

- Learning Objectives
- Prognostic Factors
- Staging And Risk Stratification
- Summary
- Progress Check

Upon completion of this module, you should be able to:

- List the assessments used to evaluate prognostic factors
- Discuss the staging workup for MCL
- Identify the scoring for risk stratification in MCL





This module will present the factors that affect prognosis, as well as the systems used to stratify patients according to risk and stage of MCL progression.

Upon completion of this module, you should be able to:

PROGNOSTIC FACTORS

- Identify the patient and disease factors that may impact the prognosis of MCL

STAGING and RISK STRATIFICATION

- Discuss the systems used to stage and stratify patients with MCL



Patient Stratification

Prognostic Factors



Assessments performed during the diagnostic workup may provide important prognostic information.¹

Factor	Effect on prognosis
 Ki-67 proliferation index ^{1,2}	A Ki67 proliferation index of $\geq 30\%$ is associated with a poor prognosis, whereas $\leq 10\%$ is associated with an indolent disease course ^{1,2}
 Age ³	Patients aged > 60 years have a worse prognosis than patients aged ≤ 60 years ³
 Stage of disease ³	Patients with stage III or IV lymphoma have a worse prognosis than patients with stage I or II lymphoma ³
 Spread of disease ³	MCL that has spread outside of the lymph nodes is associated with a worse prognosis than MCL that is contained within the lymph nodes ³
 Eastern Cooperative Oncology Group (ECOG) performance status ³	Patients with low activity levels who require help performing daily activities have a worse prognosis than active patients ³
 LDH levels ³	High LDH levels are associated with a poor prognosis ³
 WBC levels ¹	High WBC levels are associated with a poor prognosis ¹



Assessments performed during the diagnostic workup may provide important prognostic information.¹

Factor	Effect on prognosis
 Proliferation Index	A proliferation index is a measure of the number of proliferating cells in a tumour. This in turn indicates the speed (aggressiveness) of tumour growth.⁴ Ki67 is an indicator of cell proliferation and is the most established and powerful prognostic factor in MCL:^{1,4,5} • A high Ki67 proliferation index indicates a larger proportion of actively dividing lymphoma cells and a faster-growing cancer — Therefore a high Ki67 proliferation index is associated with a worse prognosis²
 ECOG performance status³	
 LDH levels³	High LDH levels are associated with a poor prognosis ³
 WBC levels¹	High WBC levels are associated with a poor prognosis ¹

Assessments per information.¹

Factor

Ki67 **prolife**
index^{1,2}

Age³

Stage of dis

Spread of d

Eastern Co
Oncology
(ECOG) pe
status³

LDH levels³

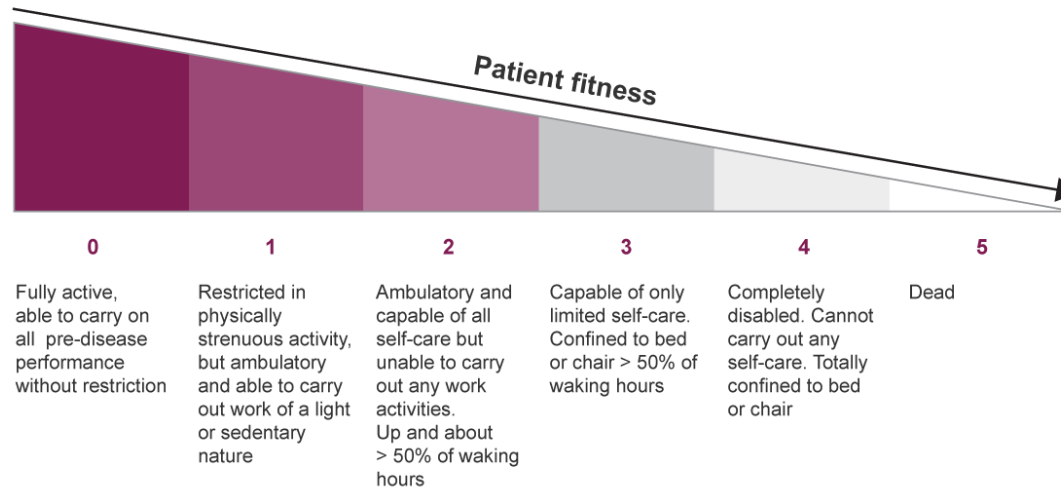
WBC levels¹

High LDH levels are associated with a poor prognosis³

High WBC levels are associated with a poor prognosis¹

ECOG Performance Status

- The ECOG performance status classifies patients based on their ability to function independently.⁶
 - ECOG performance status ranges from a grade of 0 to 5, according to increasing disability:



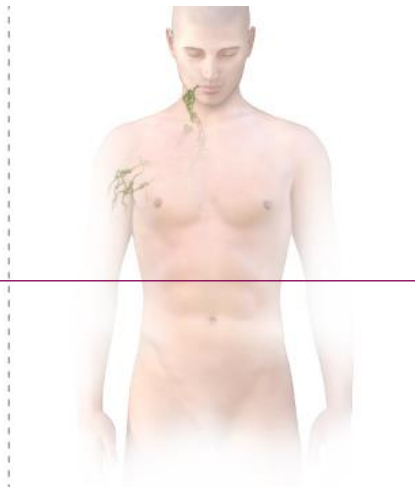
Staging

Staging is the determination of the extent to which the cancer has spread. MCL is staged using the Ann Arbor staging system, which is also used to stage other NHL types and is not specific to MCL:^{3,7}



Stage I

The lymphoma is restricted to 1 lymph node or a single region³



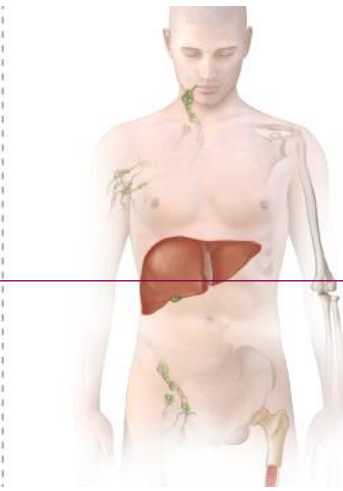
Stage II

The lymphoma is in ≥ 2 regions on the same side of the diaphragm³



Stage III

The lymphoma is in the lymph nodes, the spleen, or a nearby organ on both sides of the diaphragm³



Stage IV

The lymphoma has spread to an organ outside of the lymphatic system that is not adjacent to an involved lymph node, such as the bone marrow, liver, brain, spinal cord, or lining of the lungs³

Diaphragm



Staging

Staging is the determination of the extent to which the cancer has spread. MCL is staged using the Ann Arbor staging system, which is also used to stage other NHL types and is not specific to MCL:^{3,7}

Staging

MCL typically presents as advanced disease, with 90% of cases being stage III or IV.⁸

X



Diaphragm

Stage I

The lymphoma is restricted to 1 lymph node or a single region³

Stage II

The lymphoma is in ≥ 2 regions on the same side of the diaphragm³

Stage III

The lymphoma is in the lymph nodes, the spleen, or a nearby organ on both sides of the diaphragm³

Stage IV

The lymphoma has spread to an organ outside of the lymphatic system that is not adjacent to an involved lymph node, such as the bone marrow, liver, brain, spinal cord, or lining of the lungs³



Risk Stratification – MIPI

Patient outcome can be predicted using a prognostic index that incorporates various patient- and disease-specific factors.³

- The **Mantle Cell Lymphoma International Prognostic Index (MIPI)** is a **risk stratification** system which incorporates 4 independent prognostic factors that are associated with **overall survival (OS)**⁹
 - The MIPI score is calculated based on:



Age



ECOG performance
status



LDH levels



WBC count

Patients are stratified according to their MIPI score:⁹

MIPI score	Risk group	Median OS
< 5.7	Low risk	N/A*
5.7 to < 6.2	Intermediate risk	51 months
≥ 6.2	High risk	29 months

*Median OS was not reached in the low-risk group, with a 5-year OS of 60%.



Risk Stratification – MIPI

Patient outcome can be predicted using a prognostic index that incorporates various patient- and disease-specific factors.³

- The **Mantle Cell** **stratification** system is associated with clinical outcomes.
 - The MIPI score



Age

MIPI Score

- The MIPI score is calculated according to the following formula:⁹

$$\begin{aligned} \text{MIPI score} = & [0.03535 \times \text{age (years)} \times \text{age (years)}] \\ & + 0.6978 \text{ (if ECOG} > 1) \\ & + [1.367 \times \log_{10}(\text{LDH/upper limit of normal [ULN]})] \\ & + [0.9393 \times \log_{10}(\text{WBC count})] \end{aligned}$$

Where $\log_{10}(x)$ is the logarithm of x with base 10
(eg, $\log_{10}(100) = 2$)

Patients are stratified according to their MIPI score:⁹

MIPI score	Risk group	Median OS
< 5.7	Low risk	N/A*
5.7 to < 6.2	Intermediate risk	51 months
≥ 6.2	High risk	29 months

*Median OS was not reached in the low-risk group, with a 5-year OS of 60%.

X

a **risk**
factors that are

count



Risk Stratification – sMIPI

The Mantle Cell Lymphoma International Prognostic Index (sMIPI) was developed to facilitate the clinical application of the MIPI and bedside use.⁹

- The sMIPI uses a points system (0–3) instead of a formula to stratify patients. Points are assigned based on the 4 prognostic factors that compose the MIPI system:⁹

Points	Age	Activity level	LDH level/ULN	WBC count (10 ⁹ cells/L)
0	< 50	0–1: High: Able to perform daily tasks	< 0.67	< 6.700
1	50–59	–	0.67–0.99	6.700–9.999
2	60–69	2–4: Low: Unable to work/bedridden	1.000–1.49	1.000–14.999
3	≥ 70	–	≥ 1.5000	≥ 15000

- The points are added up, and patients are classified according to 3 risk groups:⁹

Points	Risk group	Median OS
0–3	Low risk	N/A*
4–5	Intermediate risk	51 months
6–11	High risk	29 months

*Median OS was not reached in the low-risk group, with a 5-year OS of 60%.



Risk Stratification – MIPI-c

Ki67 expression is an established prognostic factor in MCL.¹

The Combined Mantle Cell Lymphoma International Prognostic Index (MIPI-c) incorporates the Ki67 proliferation index:⁵

- The MIPI-c has improved stratification power because of the added prognostic ability of Ki67
- MIPI-c stratifies patients into 4 risk groups:



Risk group ⁵	Median survival time ⁵	5-year survival rate ⁵
Low risk	9.4 years	85%
Low-intermediate risk	4.9 years	72%
Intermediate-high risk	3.2 years	43%
High risk	1.8 years	17%



Newly designed clinical trials currently use the MIPI-c to stratify patients.^{5,10}





PROGNOSTIC FACTORS

- The prognosis of MCL is influenced by:
 - Ki67 proliferation
 - Age
 - Stage of the disease
 - Spread of the disease
 - ECOG performance status
 - LDH levels
 - WBC levels

STAGING and RISK STRATIFICATION

- MCL is staged using the Ann Arbor staging system, with stages ranging from I to IV
- MCL patients are stratified according to their risk level using the MIPI, SMIPI, or MIPI-c systems





1. Which of the following factors is associated with a worse prognosis in patients with MCL?

A) Able to perform daily activities independently

B) Age of < 60 years

C) High Ki67 proliferation index ($\geq 30\%$)

D) Lymphoma contained within the lymph nodes only





1. Which of the following factors is associated with a worse prognosis in patients with MCL?

A) Able to perform daily activities independently

B) Age of < 60 years

C) High Ki67 proliferation index ($\geq 30\%$)

D) Lymphoma contained within the lymph nodes only

C) A high Ki67 proliferation index ($\geq 30\%$) is associated with a worse prognosis in patients with MCL.





2. Alison has MCL that is localised to 2 different sets of lymph nodes in the upper part of her body. What stage is Alison's MCL?

A) Stage I

B) Stage II

C) Stage III

D) Stage IV





2. Alison has MCL that is localised to 2 different sets of lymph nodes in the upper part of her body. What stage is Alison's MCL?

A) Stage I

B) Stage II

C) Stage III

D) Stage IV

B) Alison has stage II MCL.





3. The MIPI stratifies patients based on which of the following prognostic factors?

A) Age, ECOG performance status, Ki67 proliferation index, and WBC count

B) Age, ECOG performance status, LDH levels, and RBC count

C) Age, ECOG performance status, LDH levels, and WBC count

D) Age, spread of disease, Ki67 proliferation index, and WBC count





3. The MIPI stratifies patients based on which of the following prognostic factors?

A) Age, ECOG performance status, Ki67 proliferation index, and WBC count

B) Age, ECOG performance status, LDH levels, and RBC count

C) Age, ECOG performance status, LDH levels, and WBC count

D) Age, spread of disease, Ki67 proliferation index, and WBC count

C) The MIPI stratifies patients based on age, ECOG performance status, LDH levels, and WBC count.





4. Raphael was recently diagnosed with MCL and has a sMIPI score of 8 points. Into which risk group does Raphael fit?

A) Low risk

B) Intermediate risk

C) Intermediate-high risk

D) High risk





4. Raphael was recently diagnosed with MCL and has a sMIPI score of 8 points. Into which risk group does Raphael fit?

A) Low risk

B) Intermediate risk

C) Intermediate-high risk

D) High risk

D) With a sMIPI score of 8 points, Raphael fits into the high-risk group.





5. Which of the following prognostic indices incorporates the Ki67 proliferation index for risk stratification of patients with MCL?

A) Ann Arbor

B) MIPI

C) MIPI-c

D) sMIPI





5. Which of the following prognostic indices incorporates the Ki67 proliferation index for risk stratification of patients with MCL?

A) Ann Arbor

B) MIPI

C) MIPI-c

D) sMIPI

C) The MIPI-c incorporates the Ki67 proliferation index for risk stratification of patients with MCL.



Glossary

Select the definition to return.



Eastern Cooperative Oncology Group (ECOG) performance status

A measure of patient functional status. The ECOG categorises patients into 6 grades based on their ability to independently function in daily activities.⁶

Ki67

An antigen whose expression is associated with cell proliferation.¹

Mantle Cell Lymphoma International Prognostic Index (MIPI)

A scoring system based on 4 independent factors that correlate with prognosis. The MIPI is used to plan treatment for patients with MCL.⁷

Overall survival (OS)

The length of time after diagnosis or start of treatment that patients are still alive.⁴

Proliferation index

A measure of the number of proliferating cells in a tumour. The proliferation index indicates the speed of tumour growth.⁴

Risk stratification

A formal estimate of the probability of a person succumbing to a disease or benefiting from a treatment.⁵

Staging

The process of classifying tumours, especially malignant tumours, according to tumour differentiation, potential therapeutic response, and patient prognosis.¹¹





References

1. Dreyling M, Geisler C, Hermine O, et al. Newly diagnosed and relapsed mantle cell lymphoma: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol*. 2014;25 Suppl 3:iii83-iii92.
2. Zelenetz AD, Gordon LI, Abramson JS, et al. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®). B-Cell Lymphomas. V.5.2021. National Comprehensive Cancer Network®. September 2021:1-316.
3. Non-Hodgkin Lymphoma. Atlanta, GA. American Cancer Society (ACS). February 2016:1-75.
4. National Cancer Institute (NCI). *NCI Dictionary of Cancer Terms*. Bethesda, MD: National Institutes of Health (NIH); 2016.
5. Hoster E, Rosenwald A, Berger F, et al. Prognostic value of Ki-67 index, cytology, and growth pattern in mantle-cell lymphoma: results from randomized trials of the European mantle cell lymphoma network. *J Clin Oncol*. 2016;34(12):1386-1394.
6. ECOG Performance Status. Eastern Cooperative Oncology Group (ECOG)-ACRIN Cancer Research Group. 2015;1-2.
7. Mantle Cell Lymphoma Facts. Leukaemia & Lymphoma Society. November 2014:1-9.
8. Herrero-Vicent C, Machado I, Illueca C, et al. Diagnostic and therapeutic update of mantle cell lymphoma (MCL): analysis seven cases treated in a centre in one year. *ecancermedicalscience*. 2016;10:627.
9. Hoster E, Dreyling M, Klapper W, et al. A new prognostic index (MIPI) for patients with advanced-stage mantle cell lymphoma. *Blood*. 2008;111(2):558-565.
10. Chuang WY, Chang H, Chang GJ, et al. Pleomorphic mantle cell lymphoma morphologically mimicking diffuse large B-cell lymphoma: common cyclin D1 negativity and a simple immunohistochemical algorithm to avoid the diagnostic pitfall. *Histopathology*. 2017;70:986-999.
11. Venes D, Biderman A, Fenton B, et al, eds. *Taber's Cyclopedic Medical Dictionary*. 21st ed. Philadelphia, PA: F.A. Davis Company; 2009.

