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

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Patients with MCL commonly present with B symptoms[1,2]

Unexplained fevers
(>100.5°F)

Unintentional weight loss
(≥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 >

Clinical tria

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Asymptomatic disease/ abnormal labs

Symptom onset

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

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Initial clinical evaluation for patients consists of physical examination, gathering patient history, and conducting laboratory testing[1]

Recommended laboratory testing includes[1,6]

- CBC with differential
- LDH
- Comprehensive metabolic panel
- Hepatitis B testing

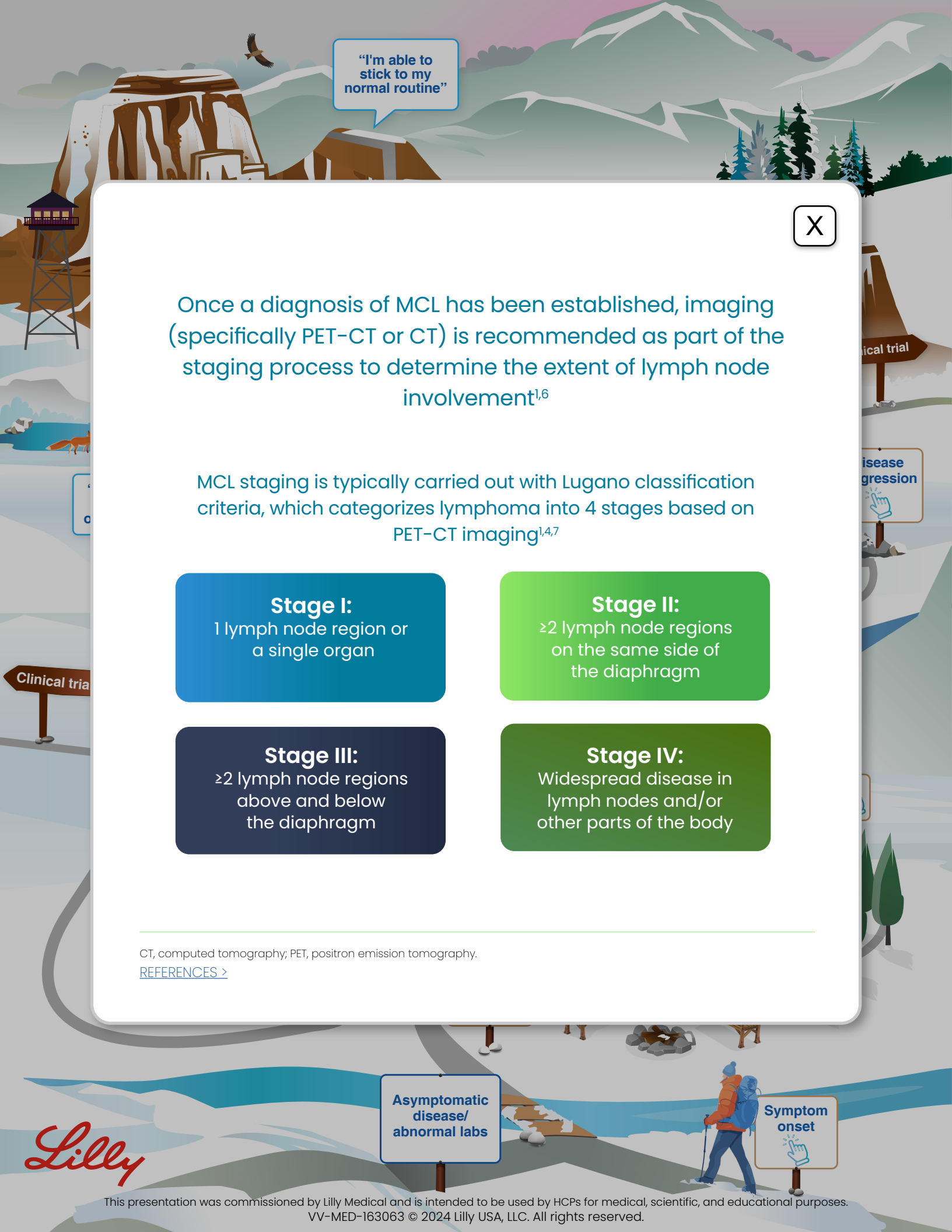
Bone marrow aspiration and tissue biopsy are conducted following laboratory testing to help establish a diagnosis of MCL, including immunohistochemistry and flow cytometry, as well as histopathologic assessment[1]

CBC, complete blood count; LDH, lactate dehydrogenase.

REFERENCES >

Asymptomatic disease/ abnormal labs

Symptom onset



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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]

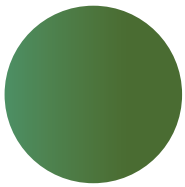
- MIPI uses factors such as age, ECOG PS, LDH levels, and WBC count to determine a patient's overall survival prognosis
- MIPI scores used in conjunction with the Ki-67 index can also determine a cumulative prognostic index (biological MIPI)

Additionally, prognosis can be determined when the following factors are considered[3]

- 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 rates[10]

Cluster 1
Mutated *IGHV, CCND1* mutation, amp(11q), and active BCR signaling

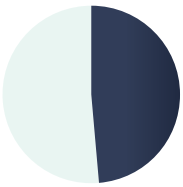


100%
5-year OS rate

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 *SP140, 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; *SP140,* Speckled 140 KDa; *TP53,* tumor protein p53; WBC, white blood cell.

REFERENCES >

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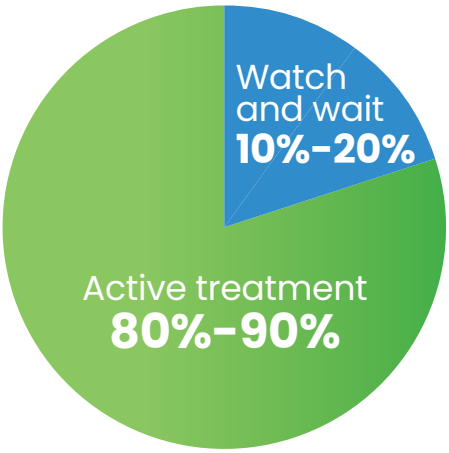
The majority of patients with MCL will move on to active treatment, whereas some patients have "smoldering" or indolent disease that requires placement into watch and wait status or a clinical trial specific to this early stage of disease[1,3]



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]

Seek patient participation

Help patients explore and compare treatment options

Assess patient values and preferences

Reach a decision with the patient

Evaluate the patient's decision

REFERENCES >

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 DISEASE[15-20]

- Chemo-immunotherapy
- CAR T-cell therapy
- Stem cell transplant
- Targeted therapy (including BTKi)

Available advanced disease treatment options by line of therapy[14-22]

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 BTKi[22]

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.

REFERENCES >

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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]

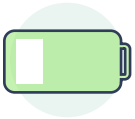
Upper respiratory tract infection/ pneumonia
(10%-39%)[21,24,26,b]

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]

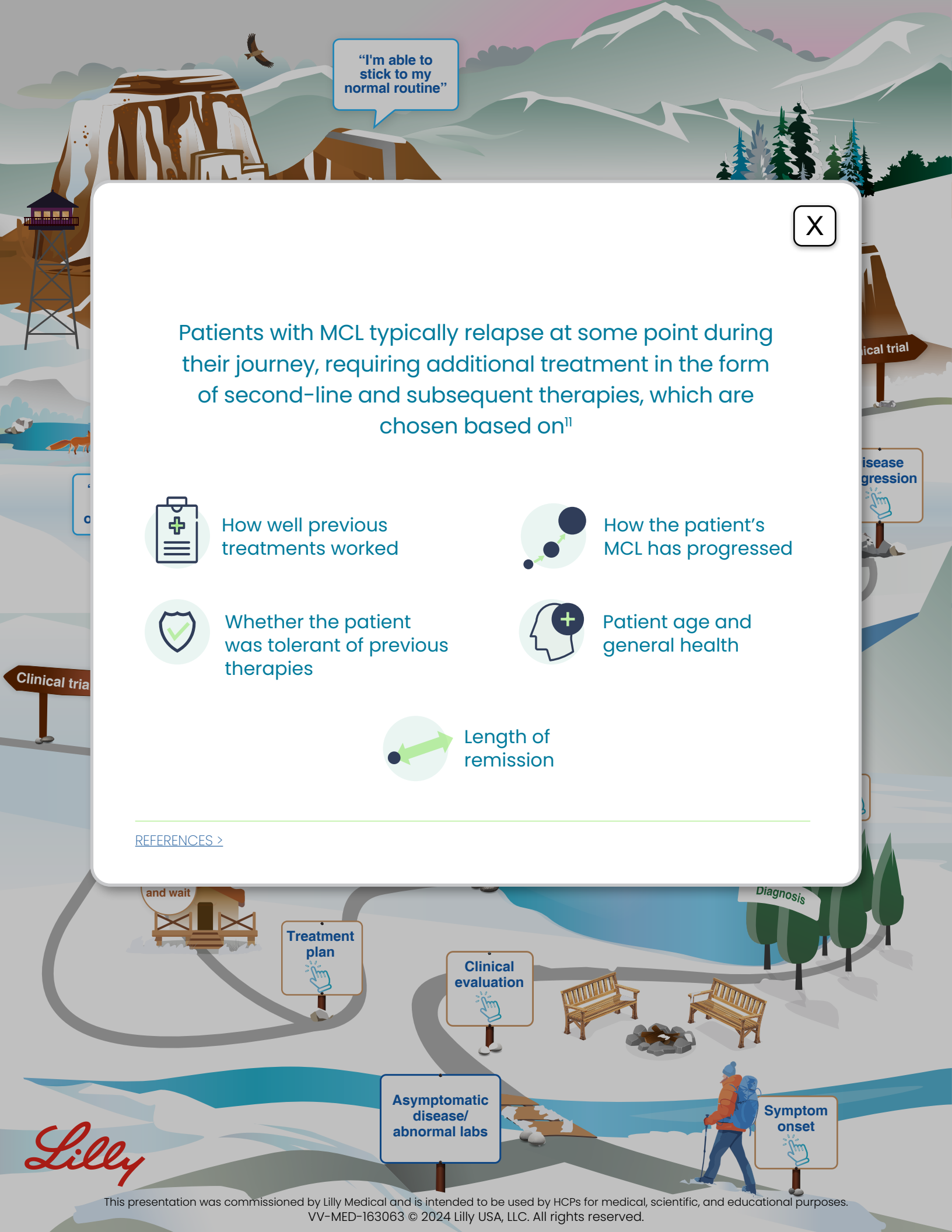
Nausea
(11%-36%)[20,21,23,25,26,d]

[a]Range based on data from patients with MCL treated with immunotherapy, and targeted therapy (proteasome inhibitors and BTK inhibitors).
[b]Range based on data from patients with MCL treated with immunotherapy and targeted therapy (BTK inhibitors).
[c]Range based on data from patients with MCL treated with immunotherapy, CAR T-cell therapy, and targeted therapy (BTK inhibitors).
[d]Range based on data from patients with MCL treated with immunotherapy, CAR T-cell therapy, and targeted therapy (proteasome inhibitors and BTK inhibitors)

REFERENCES >

Asymptomatic disease/ abnormal labs

Symptom onset



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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 on[11]

- 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

REFERENCES >