MCL Patient Journey Implementation Guide

Introduction

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Objective

- Introduce the MCL patient journey map

Introduction

- The MCL patient journey map is intended to help HCPs facilitate tailored conversations with patients as they navigate MCL diagnosis and treatment

Key Talking Points

- Assess where the patient is on their MCL journey on the map
- Briefly recap any prior steps leading up to where the patient is at this time
- Review the trigger point information specific to where the patient is currently located on their journey
- Returning to the map, provide a brief overview of next steps on the patient's MCL journey
- Pause for patient questions, highlighting the importance of the patient's role in MCL management

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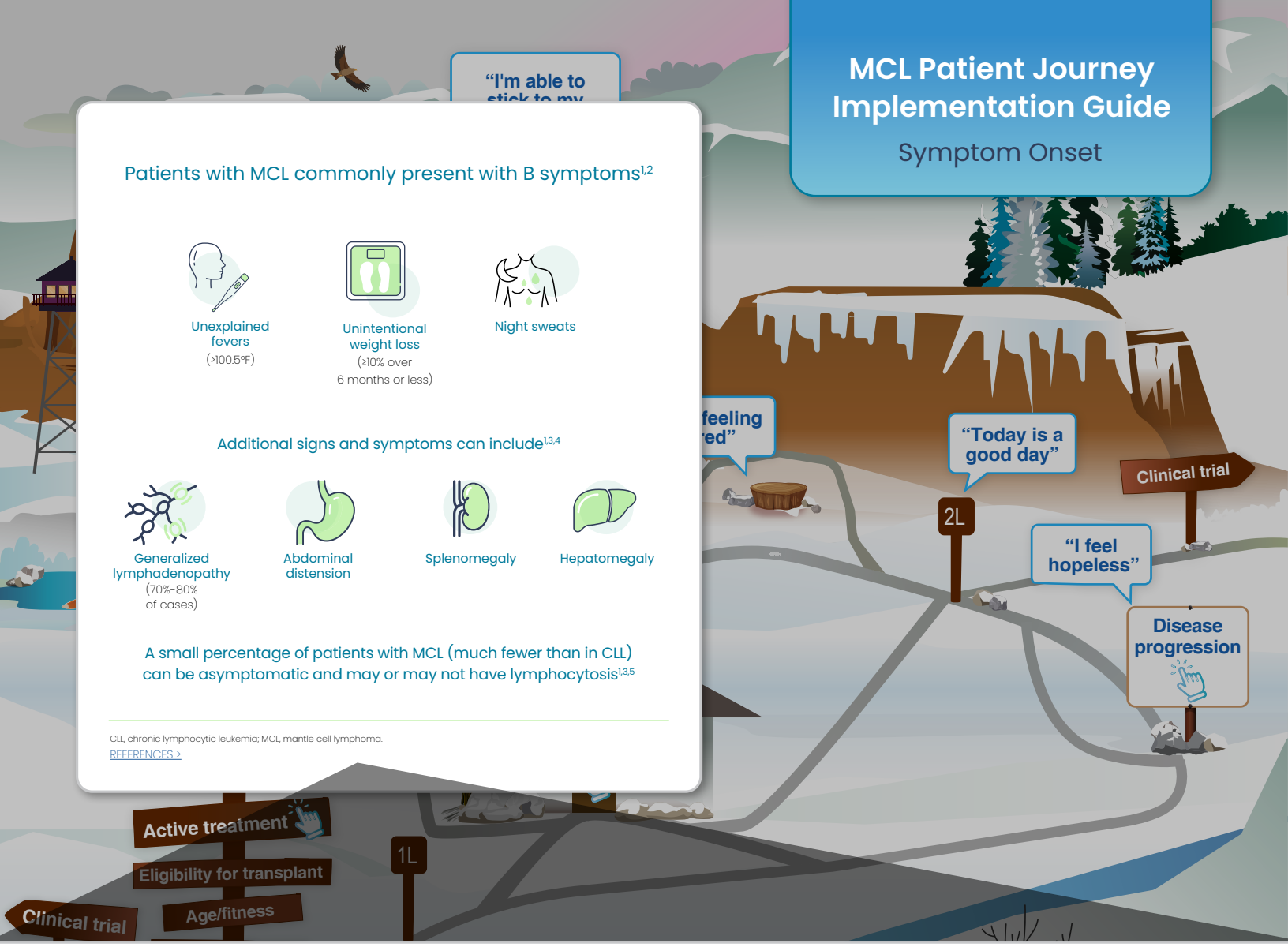
Symptom Onset



Objective

- Discuss ways in which patients may enter the MCL journey

- A patient, depicted below as a snowshoe hiker, will often begin their MCL journey by presenting with B symptoms (eg, unexplained fever, unintentional weight loss, and night sweats), as well as additional signs and symptoms. A small percentage of patients can be asymptomatic and learn of their disease through laboratory tests conducted during a routine HCP visit for an unrelated reason
- The next stopping point for the patient is initial clinical evaluation where additional testing is performed to help assist in the diagnosis and staging of MCL

Key Talking Points

- Share that patients may enter the MCL journey as a result of overt symptom onset or less commonly by abnormal laboratory values (asymptomatic)
- Review common symptoms associated with MCL
- Discuss how the patient's MCL journey began and what the next steps are
- Pause for patient questions, highlighting the importance of the patient's shared decision-making role in MCL management

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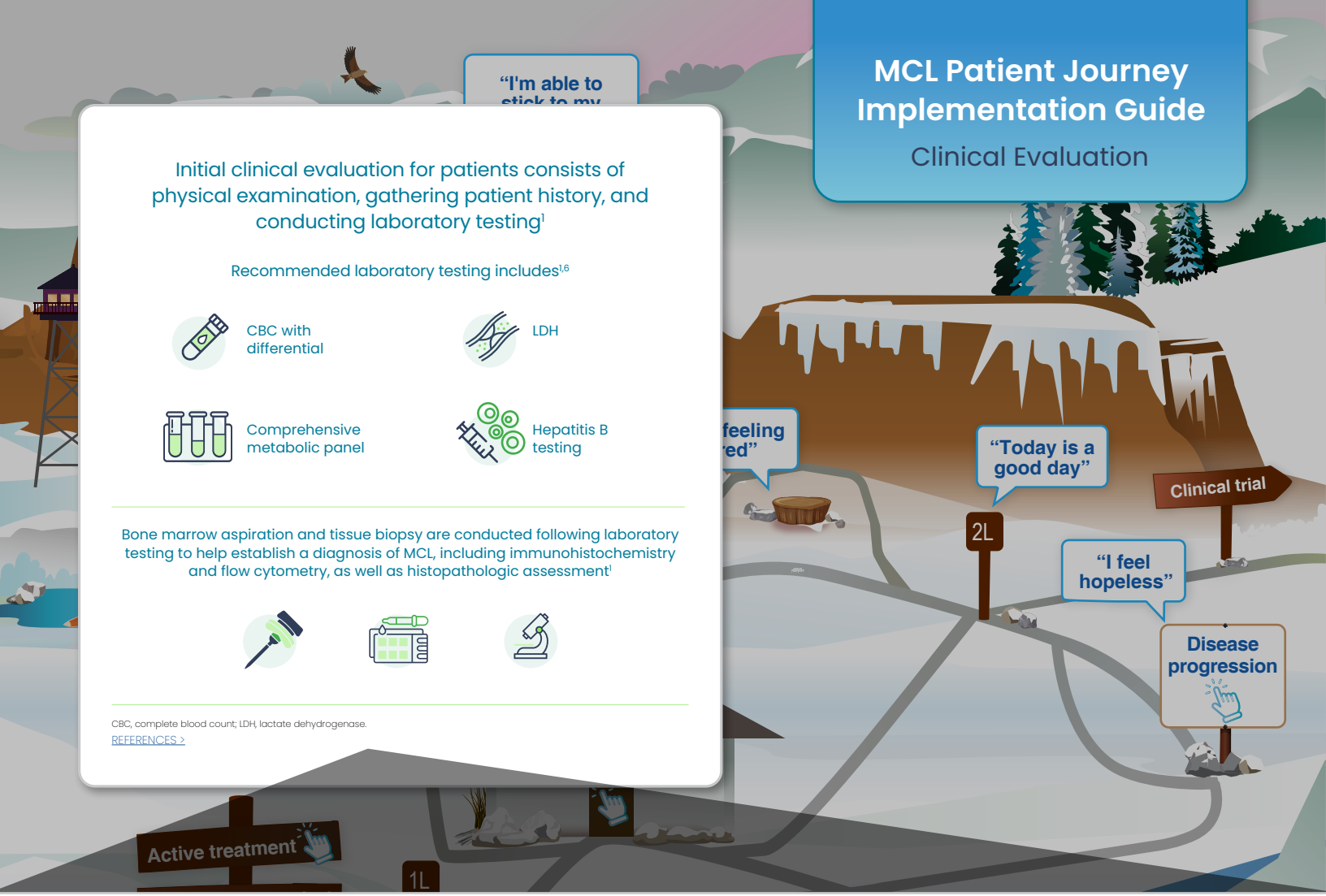
Clinical Evaluation



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Objective

- Review the various testing methods used during initial clinical evaluation of a patient with MCL

- After entering the MCL patient journey through symptomatic presentation or abnormal laboratory results, a patient will undergo initial clinical evaluation (shown here as a rest area with benches and firepit) to help determine a diagnosis
- Additional testing may include capturing the patient's health history, performing a physical examination, immunophenotyping, and laboratory testing followed by bone marrow aspiration and tissue biopsy
- The next leg of the patient journey involves receiving a diagnosis of MCL followed by staging to help the patient and their HCP understand the severity of the disease

Key Talking Points

- Review the testing and evaluation methods used to diagnose and assess MCL after patients have presented with symptoms or an abnormal laboratory finding was discovered
- Discuss which method(s) have been used for the patient and what the test results indicate
- Share any plans for additional testing, including rationale
- Provide an overview of next steps on the patient's MCL journey

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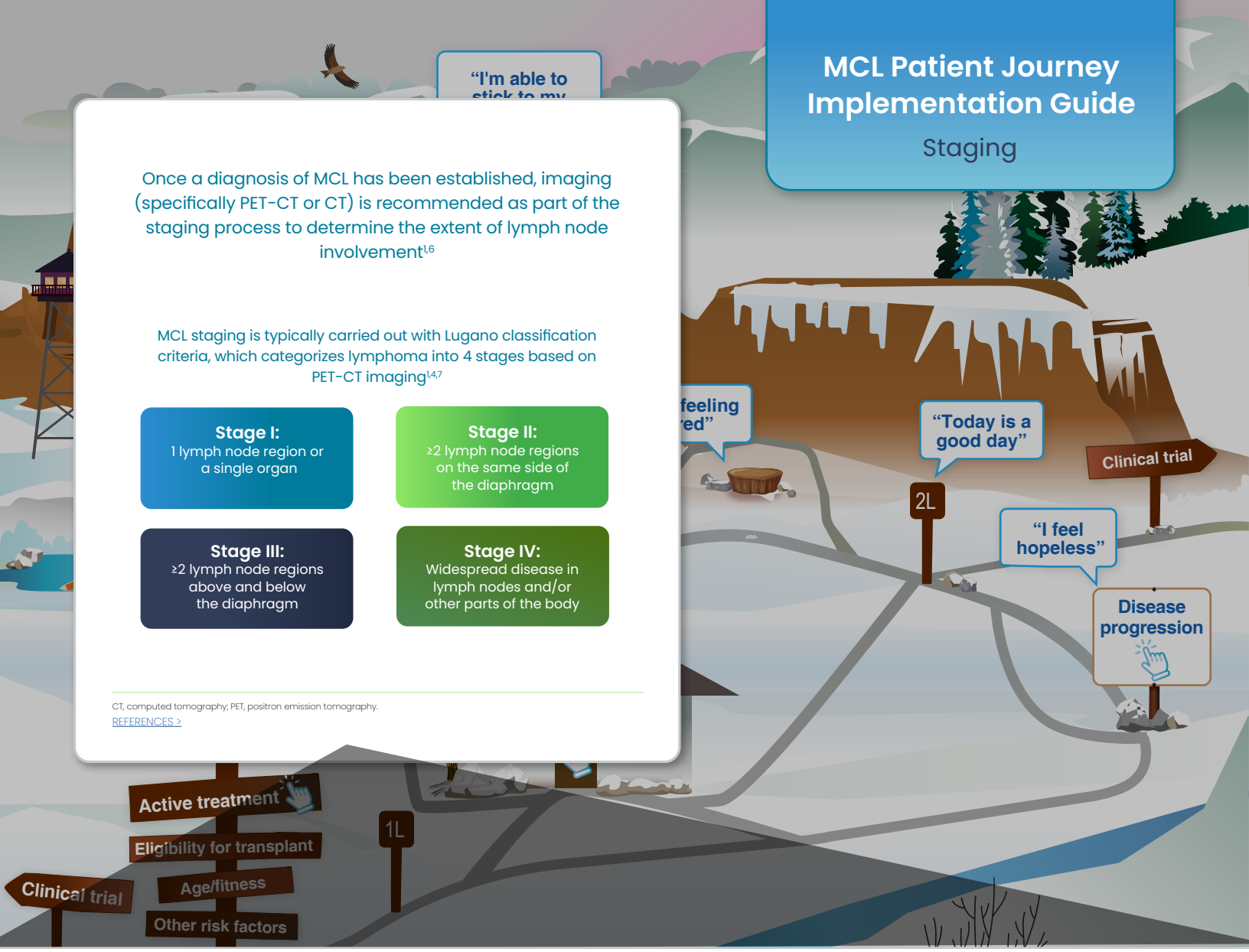
Staging



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 >

Objective

- Provide an overview of MCL staging

- After receiving a diagnosis of MCL, the patient will go through disease staging (depicted here as a snowy bridge crossing over an icy pond) to determine extent of disease
- MCL is staged with the help of imaging (specifically PET-CT or CT) to determine the extent of lymph node involvement
- Lugano classification criteria are typically used to stage MCL; includes 4 stages based on PET-CT imaging
- Once the patient's MCL has been staged, the next stop on the path is disease prognosis to help determine a patient's prospective outlook

Key Talking Points

- Educate the patient on why MCL staging is necessary, which methods are generally used, and what each assessment entails
- Discuss which method(s) will be/have been used for the patient and what the staging results indicate for their journey
- Review next steps on the patient's MCL journey

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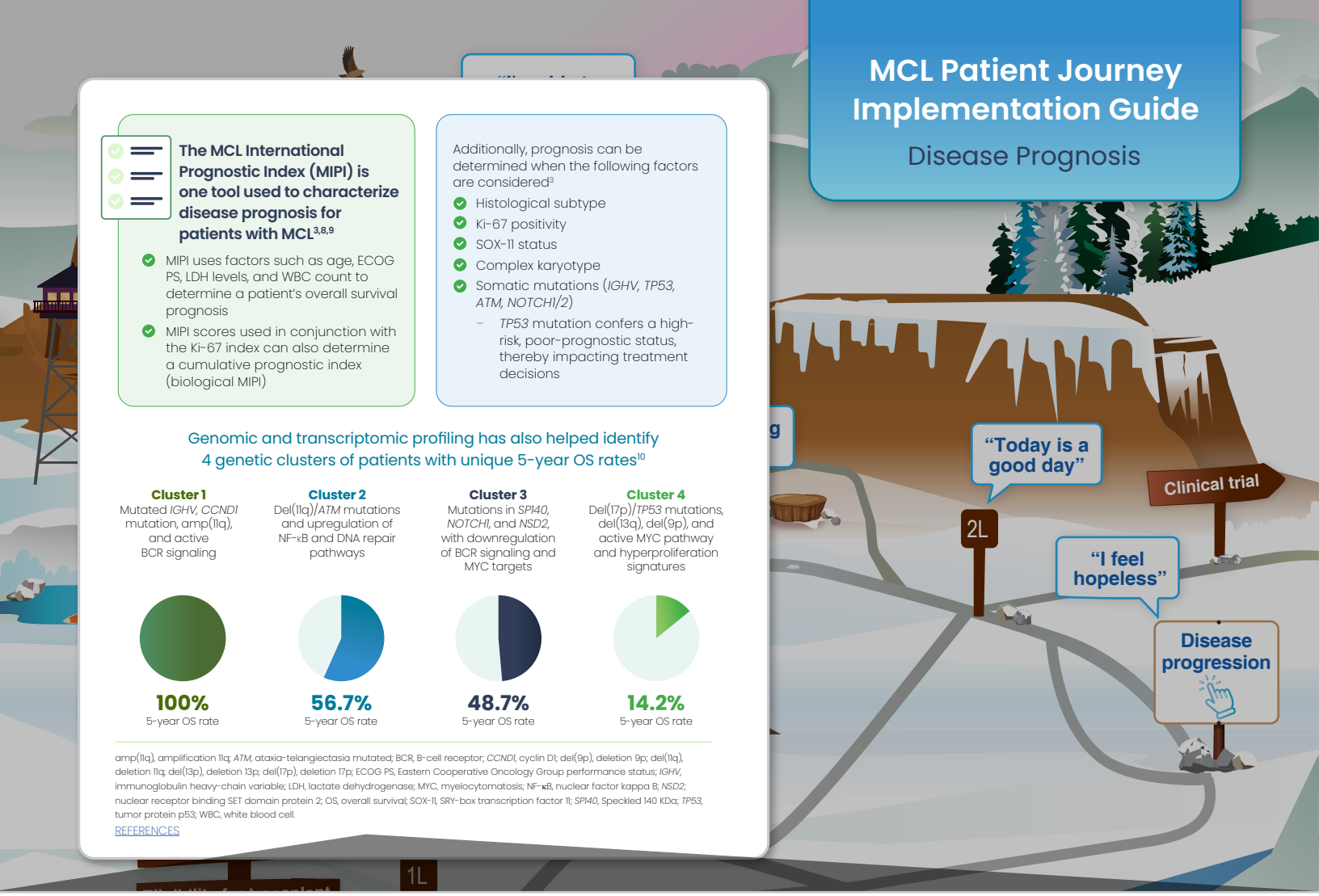
Disease Prognosis



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	**Cluster 2**	**Cluster 3**	**Cluster 4**
Mutated *IGHV, CCND1* mutation, amp(11q), and active BCR signaling	Del(11q)/*ATM* mutations and upregulation of NF-κB and DNA repair pathways	Mutations in *SPI40, NOTCH1*, and *NSD2*, with downregulation of BCR signaling and MYC targets	Del(17p)/*TP53* mutations, del(13q), del(9p), and active MYC pathway and hyperproliferation signatures
100% 5-year OS rate	**56.7%** 5-year OS rate	**48.7%** 5-year OS rate	**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.

REFERENCES

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Objective

- Provide an overview of MCL disease prognosis

- After MCL staging, the patient will undergo disease prognosis assessment (shown as a fishing platform on the bridge)
- The MCL International Prognostic Index (MIPI) uses factors such as age, ECOG PS, LDH levels, and WBC count to determine a patient's overall survival prognosis
- Coupled with MIPI scoring, the Ki-67 index is also used to determine a cumulative prognostic index, also known as a biological MIPI
- Additional factors such as histological subtype, Ki-67 positivity, SOX11 status, complex karyotype, and the presence of somatic mutations are also used to help determine patient prognosis
- Once the patient has undergone disease prognosis assessment, the next step of the journey is developing a treatment plan

Key Talking Points

- Educate the patient on why disease prognosis assessment is performed
- Review MIPI and Ki-67 index scoring, other prognostic factors, associated data, and prognostic implications
- Discuss which disease prognosis assessment the patient has undergone (if evaluation has already been completed) or provide next steps for assessment of the patient
- Review next steps on the patient's MCL journey

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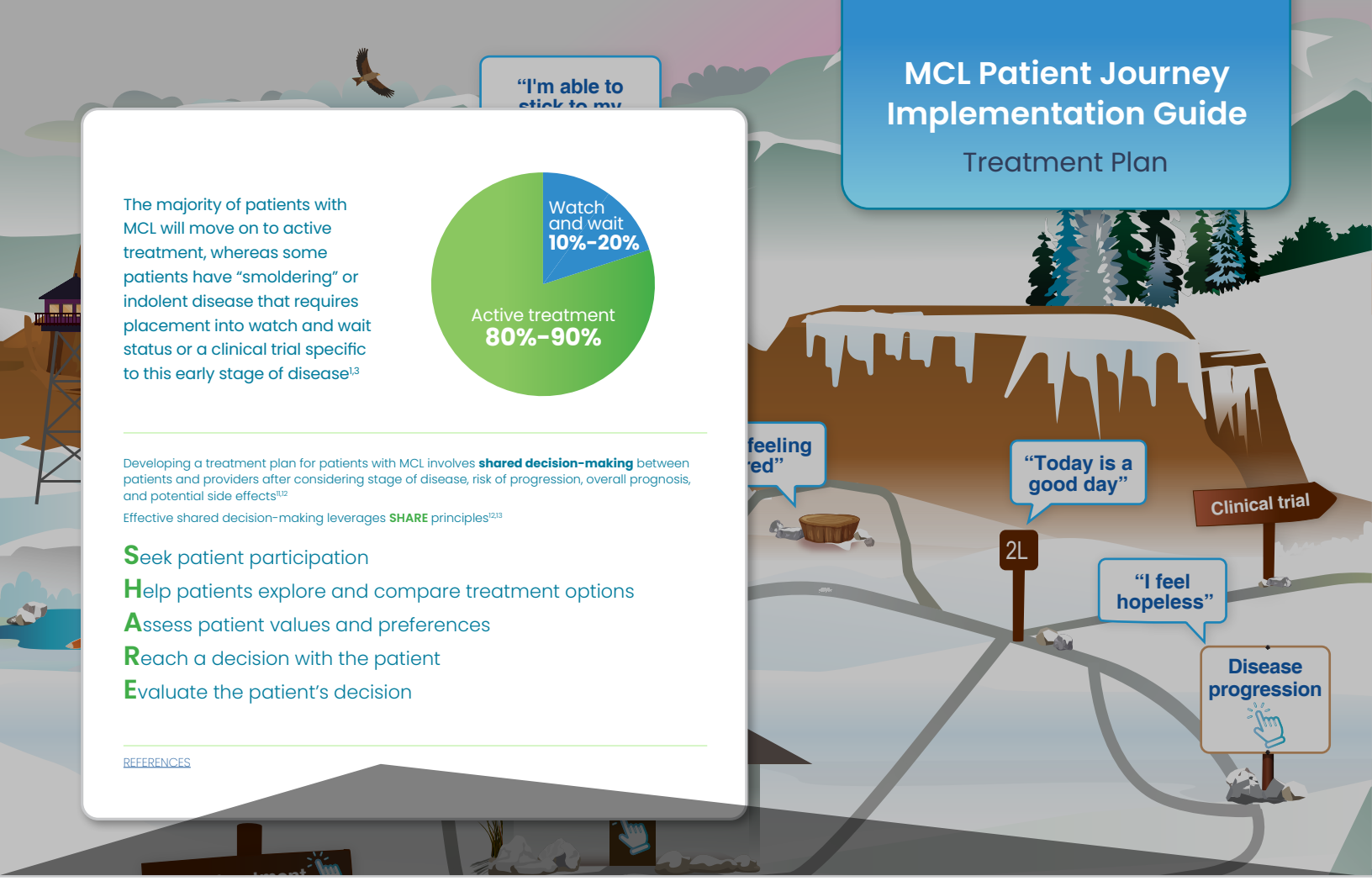
Treatment Plan



Objective

- Discuss factors that go into determining a patient's MCL treatment plan

- Once the patient and their HCP have a good understanding of the stage of disease, the MCL journey continues with the development of a treatment plan
- Developing a treatment plan involves shared decision-making between the patient and their HCP, ensuring patient preferences are considered throughout the process
- Two options exist for the next portion of the MCL journey (shown here as a forked path), where the majority (80%-90%) of patients diagnosed with MCL will immediately require active treatment (displayed as a trailhead) while some patients (10%-20%) will be placed into watch and wait status (depicted here as an inn)
- Patients who are placed into watch and wait status will eventually require treatment (shown here as the path from the inn rejoining the main path to the active treatment trailhead)

Key Talking Points

- Review the difference between active treatment vs watch and wait status, the latter referring to a period of active surveillance, where there is no treatment, but the patient is routinely assessed
- Highlight the importance of patient participation when determining the course of action for treatment and overall disease management
- Provide an overview of the patient's recommended treatment plan
- Discuss next steps in the patient's MCL journey

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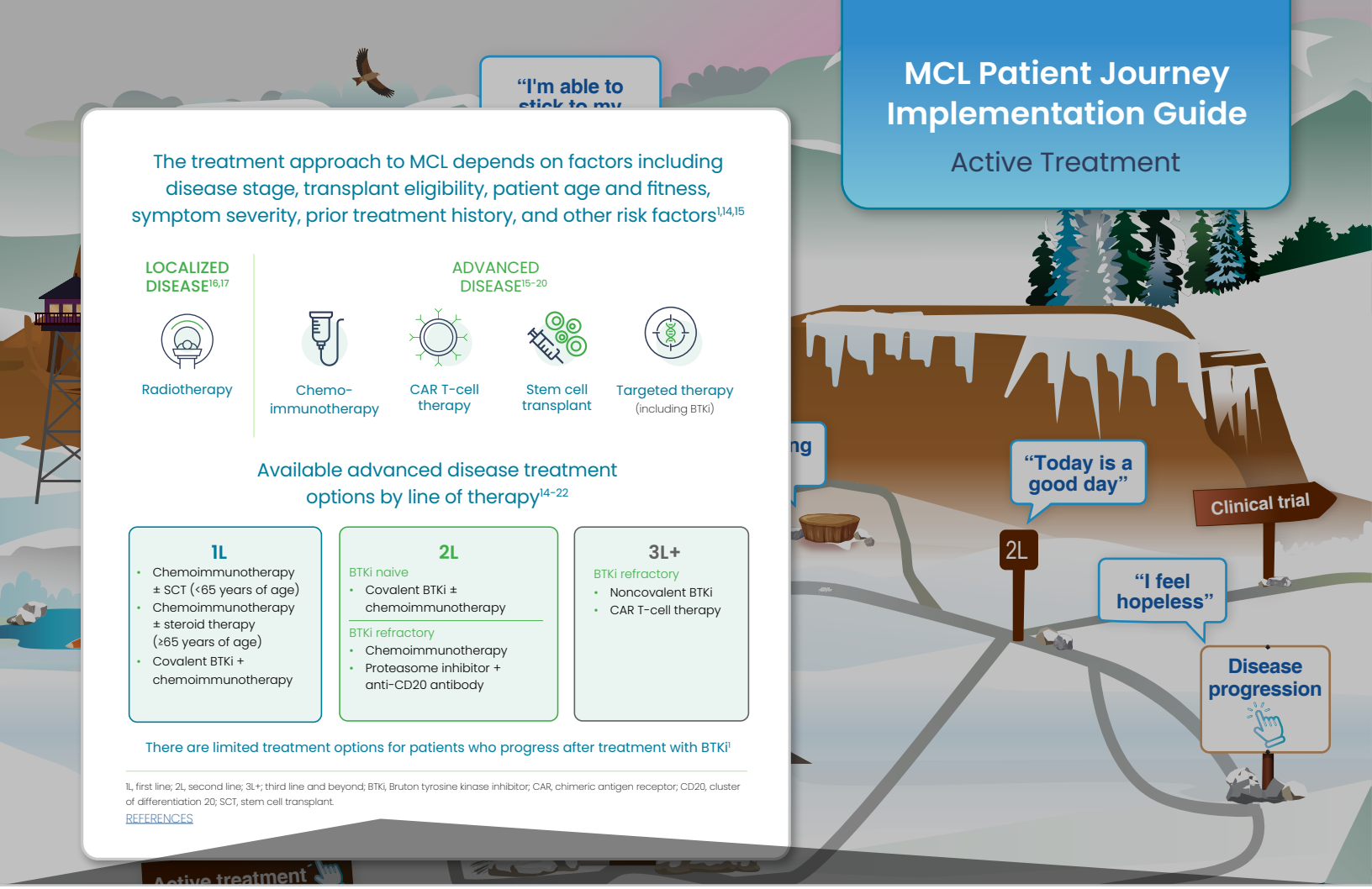
Active Treatment



Objective

- Review types of active treatment based on disease severity

- When initiating active treatment (displayed here as a trailhead), the patient is placed on a first-line therapeutic regimen based on several factors, including disease stage, transplant eligibility, age, fitness, symptom severity, prior treatment history, and other risk factors (displayed here as additional trailhead signs)
- The number of treatment options can be overwhelming for patients (indicated here by a quote, "my treatment options are overwhelming"), especially options for first-line therapy and beyond in patients with advanced disease (eg, chemoimmunotherapy, CAR T-cell therapy, stem cell transplant, and targeted therapy [including BTK inhibitors])
- In some cases, a patient may be a good candidate for a clinical trial (shown here as an alternative side path)
- As the patient continues with active treatment, they may experience adverse events and/or disease progression that require triage and/or switching to a second-line therapy

Key Talking Points

- Discuss the difference between localized and advanced MCL and review which type the patient has
- Educate the patient on the various treatment modalities associated with localized and advanced disease and the settings in which they are approved for use
- Share which treatment type(s) the patient has already or will soon be receiving
- Provide an overview of next steps in the patient's MCL journey

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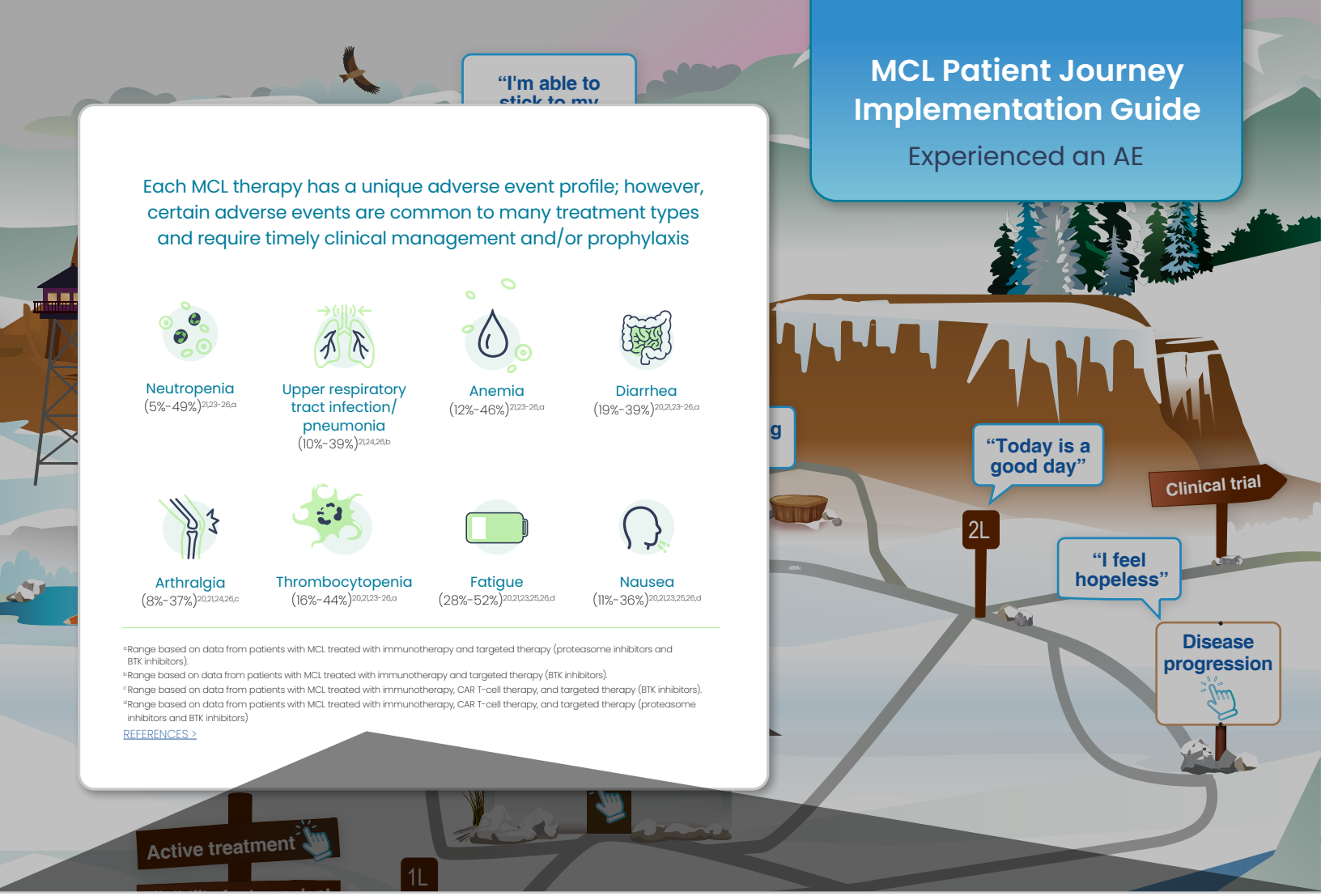
Experienced an AE



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 >

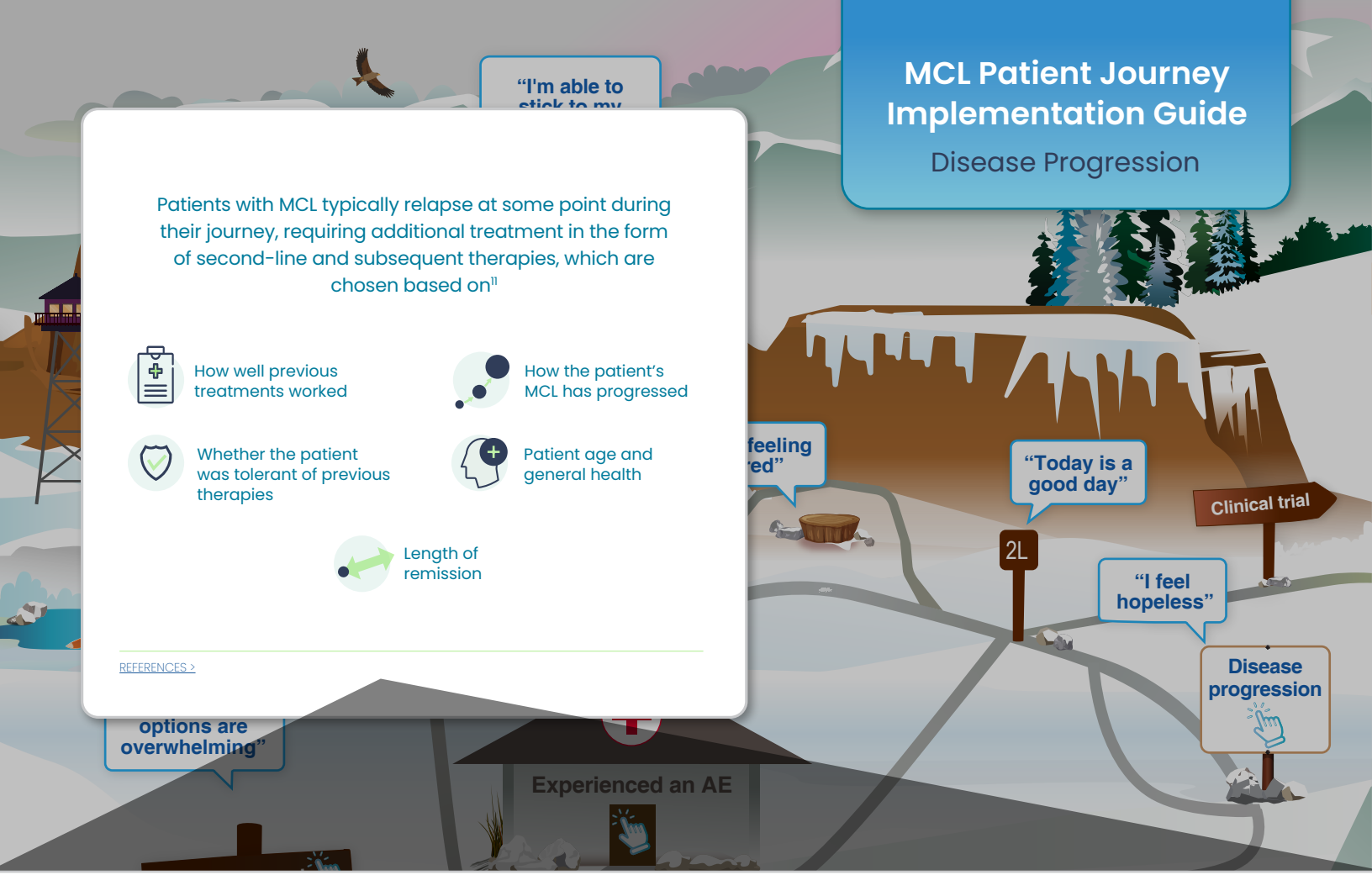
Objective

- Provide an overview of common adverse events associated with many MCL treatments

- During active treatment, regardless of line of therapy, a patient may experience adverse events (depicted here as a first aid station on a side path detour from the main path) that require additional management, dosage modification, and/or discontinuation of therapy
- Common adverse events associated with several types of MCL therapy include cytopenias, fatigue, and upper respiratory tract infections
- For patients who experience severe adverse events requiring treatment discontinuation, the next leg of the MCL patient journey likely involves being placed on a new therapeutic agent

Key Talking Points

- Educate the patient on adverse events associated with many MCL treatments, while reiterating that each MCL therapy has a unique adverse event profile
- Remind patients of the importance of reporting adverse events to their health care team
- Review any adverse events the patient may have experienced thus far, as well as how those adverse events were managed
- Provide an overview of next steps in the patient's MCL journey



Objective

- Discuss the causes of MCL disease progression

- Ultimately, a patient with MCL will likely eventually experience disease progression (shown here as an impassable rock pile) at some point during their journey, requiring a change in therapy (displayed as an alternative path around the disease progression barrier)
- Second-line and subsequent MCL therapies are typically chosen based on how well previous treatments worked, tolerance to previous therapy, history of progression, patient age and general health, as well as length of remission
- For the remainder of the journey, the patient continues to have additional treatment options, including the opportunity to enroll in a clinical trial as part of second- or third-line therapy
- Other points of interest to note are the progression of peaks and valleys of the overall journey, especially as the patient reaches second-line therapy and beyond (depicted here with quotes stating, "I'm afraid to switch treatments," "Today is a good day," "I'm feeling tired," and "I'm able to stick to my normal routine")

Key Talking Points

- Review the meaning of MCL disease progression and set expectations for the patient in terms of overall disease outlook
- Share the factors that impact how second-line and subsequent therapies are chosen
- Discuss where the patient is in their MCL journey and what next steps are in terms of deciding on a revised treatment plan