# CLL Patient Journey Implementation Guide

Introduction

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

"I am afraid to switch treatments"

Clinical trial

3L

"I'm feeling tired"

"Today is a good day"

2L

Clinical trial

"I feel hopeless"

Disease progression

Experienced an AE

"My treatment options are overwhelming"

Time-limited therapy

Continuous therapy

Clinical trial

1L

Active treatment

Biomarker testing

Staging

Watch and wait

Diagnosis

Treatment plan

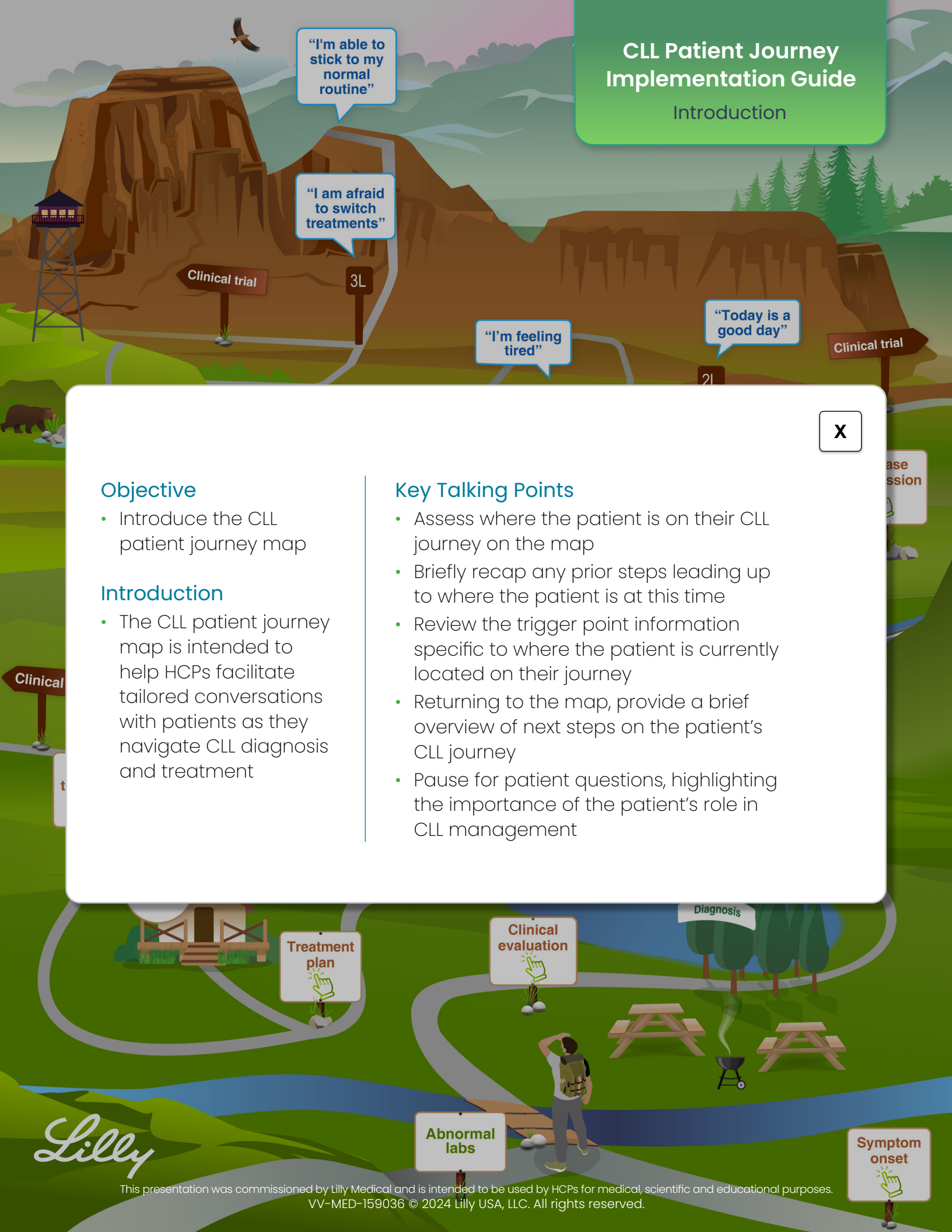
Clinical evaluation

Abnormal labs

Symptom onset

# CLL Patient Journey Implementation Guide

Introduction

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## Objective

- Introduce the CLL patient journey map

## Introduction

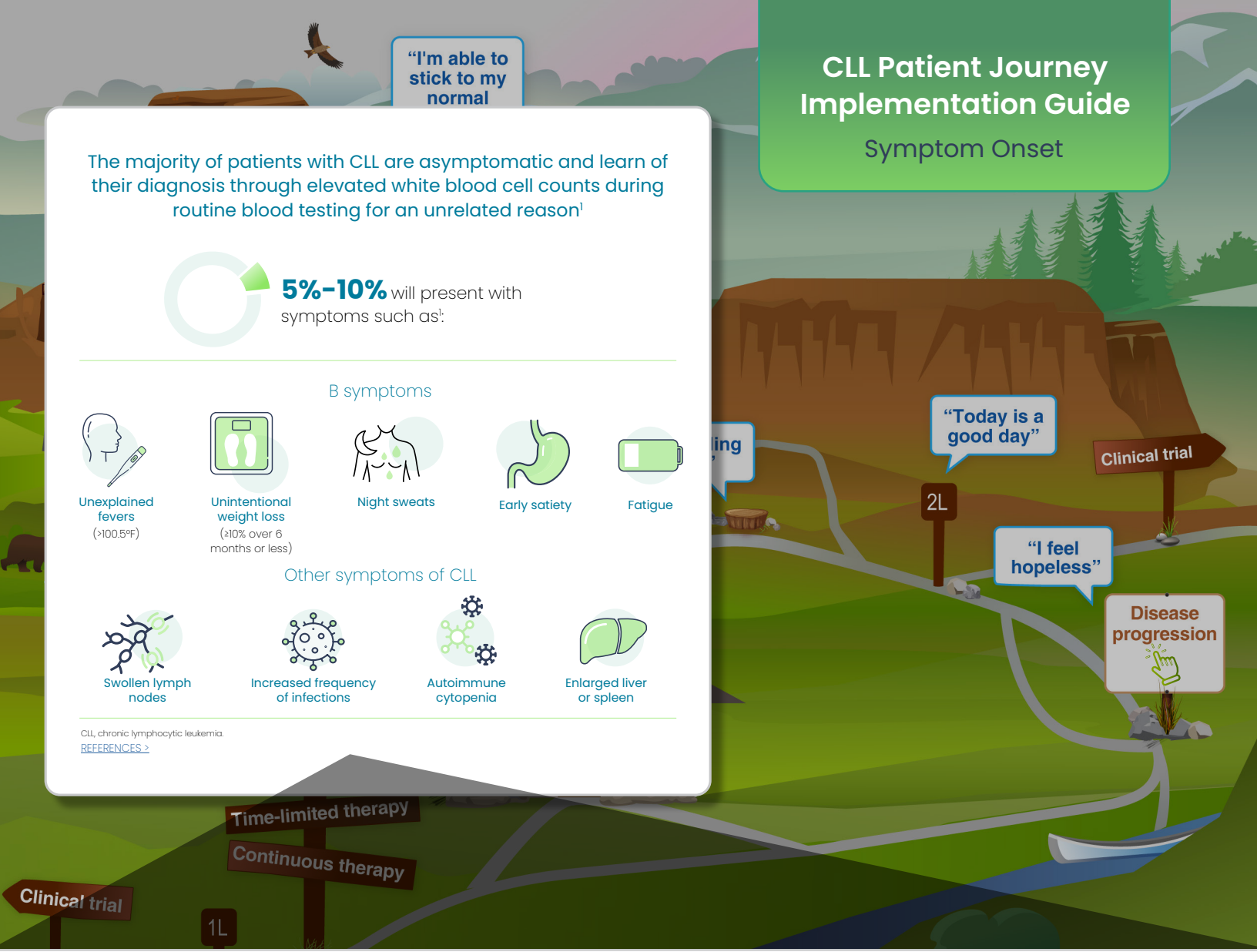
- The CLL patient journey map is intended to help HCPs facilitate tailored conversations with patients as they navigate CLL diagnosis and treatment

## Key Talking Points

- Assess where the patient is on their CLL 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 CLL journey
- Pause for patient questions, highlighting the importance of the patient's role in CLL management

# CLL Patient Journey Implementation Guide

## Symptom Onset

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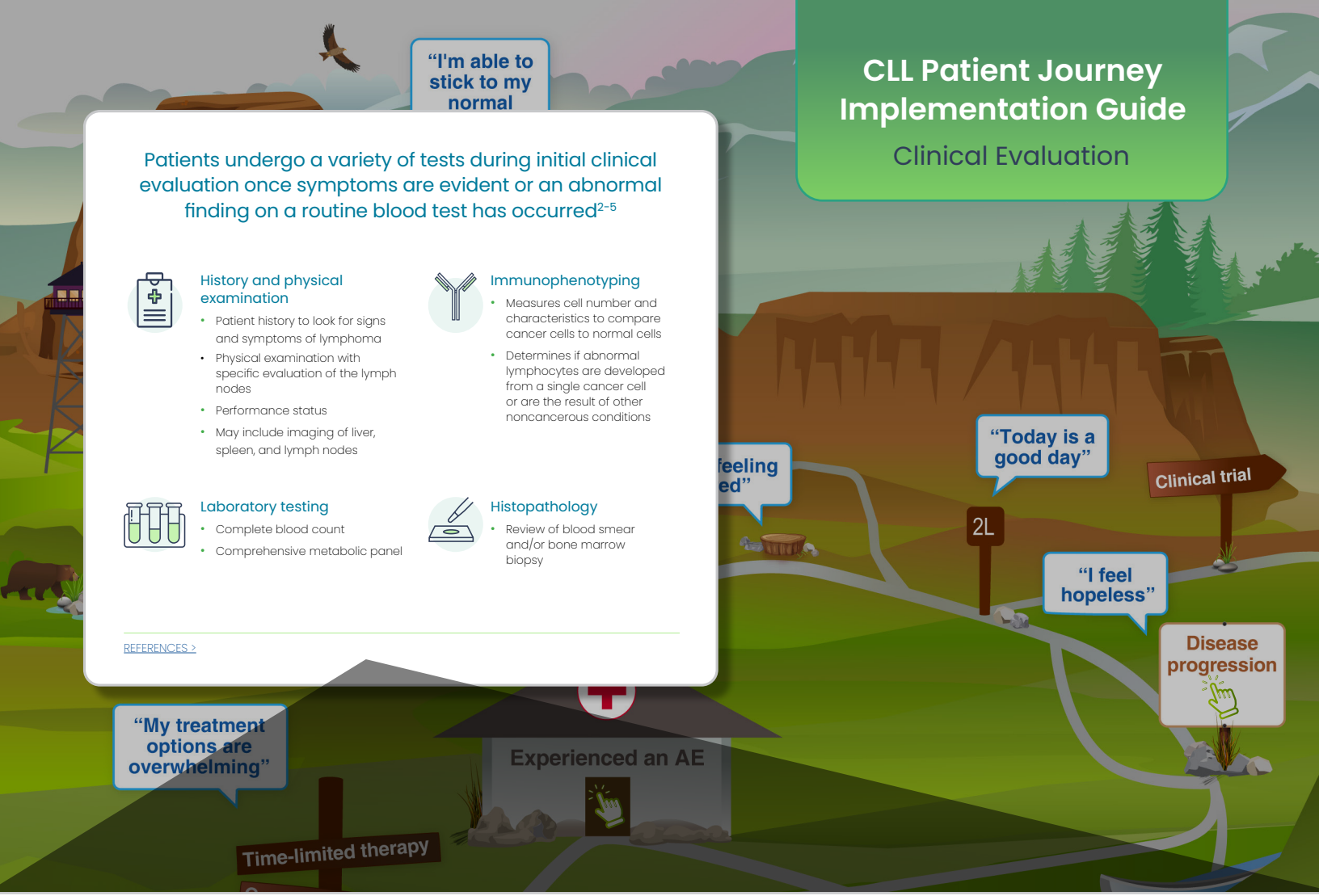
## Objective

- Discuss ways in which patients may enter the CLL journey

- A patient, depicted below as a hiker, will often begin their CLL journey as a result of abnormal blood tests conducted during a routine HCP visit for an unrelated reason or in some cases by presenting with symptomatic disease
- 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 CLL

## Key Talking Points

- Share that patients may enter the CLL journey as a result of abnormal laboratory values (asymptomatic) or by overt symptom onset
- Review common symptoms associated with CLL
- Discuss how the patient's CLL journey began and what the next steps are, preparing them for success as they navigate multiple crossroads along the way
- Pause for patient questions, highlighting the importance of the patient's shared decision-making role in CLL management

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## Objective

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

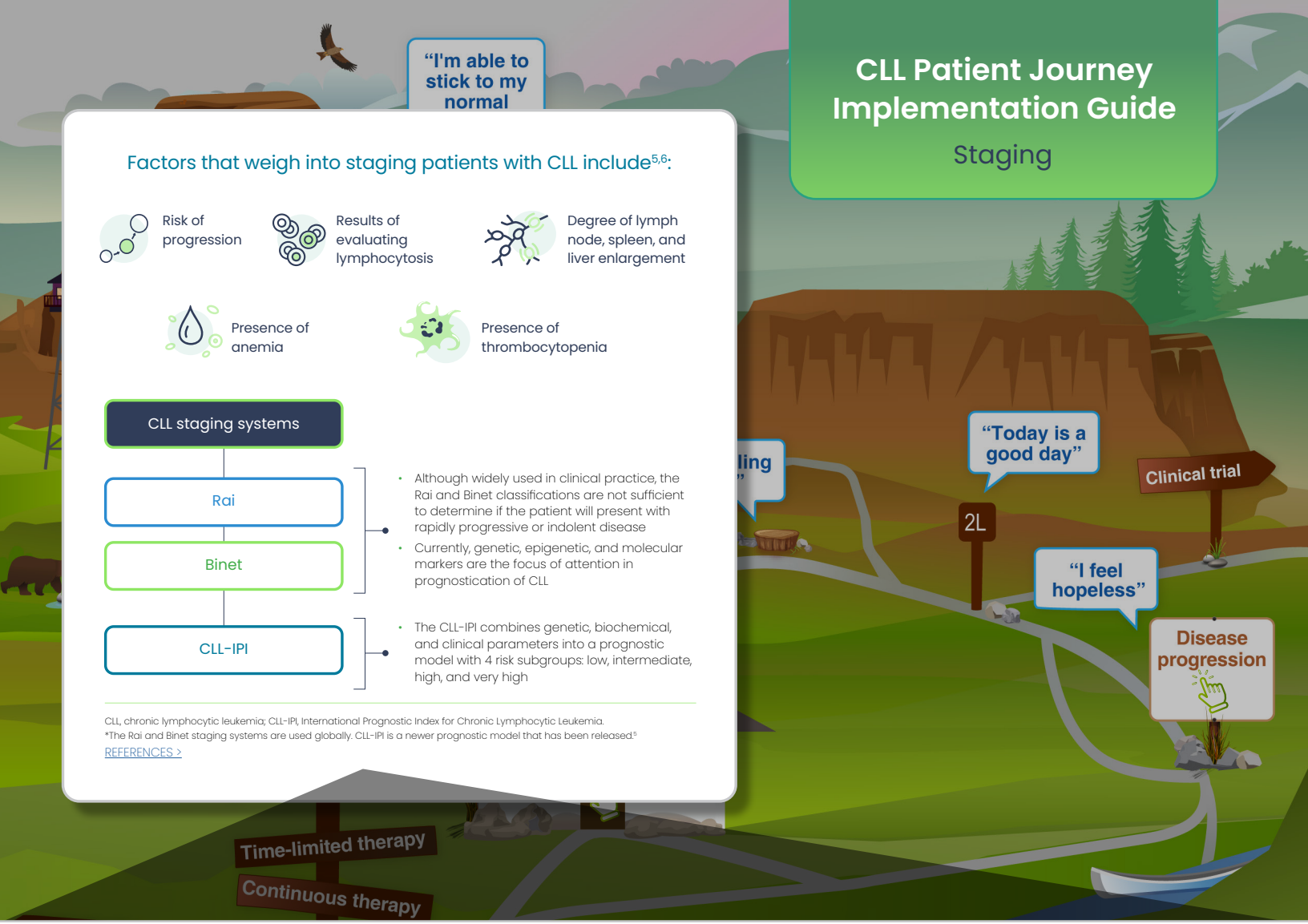
- After entering the CLL patient journey through symptomatic presentation or abnormal laboratory results, a patient will undergo initial clinical evaluation (shown here as a picnic/rest area) to help determine a diagnosis
- Additional testing may include capturing the patient's health history, performing a physical examination, immunophenotyping, laboratory testing, and histopathologic assessment
- The next leg of the patient journey involves receiving a diagnosis of CLL 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 CLL 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 CLL journey

# CLL Patient Journey Implementation Guide

## Staging



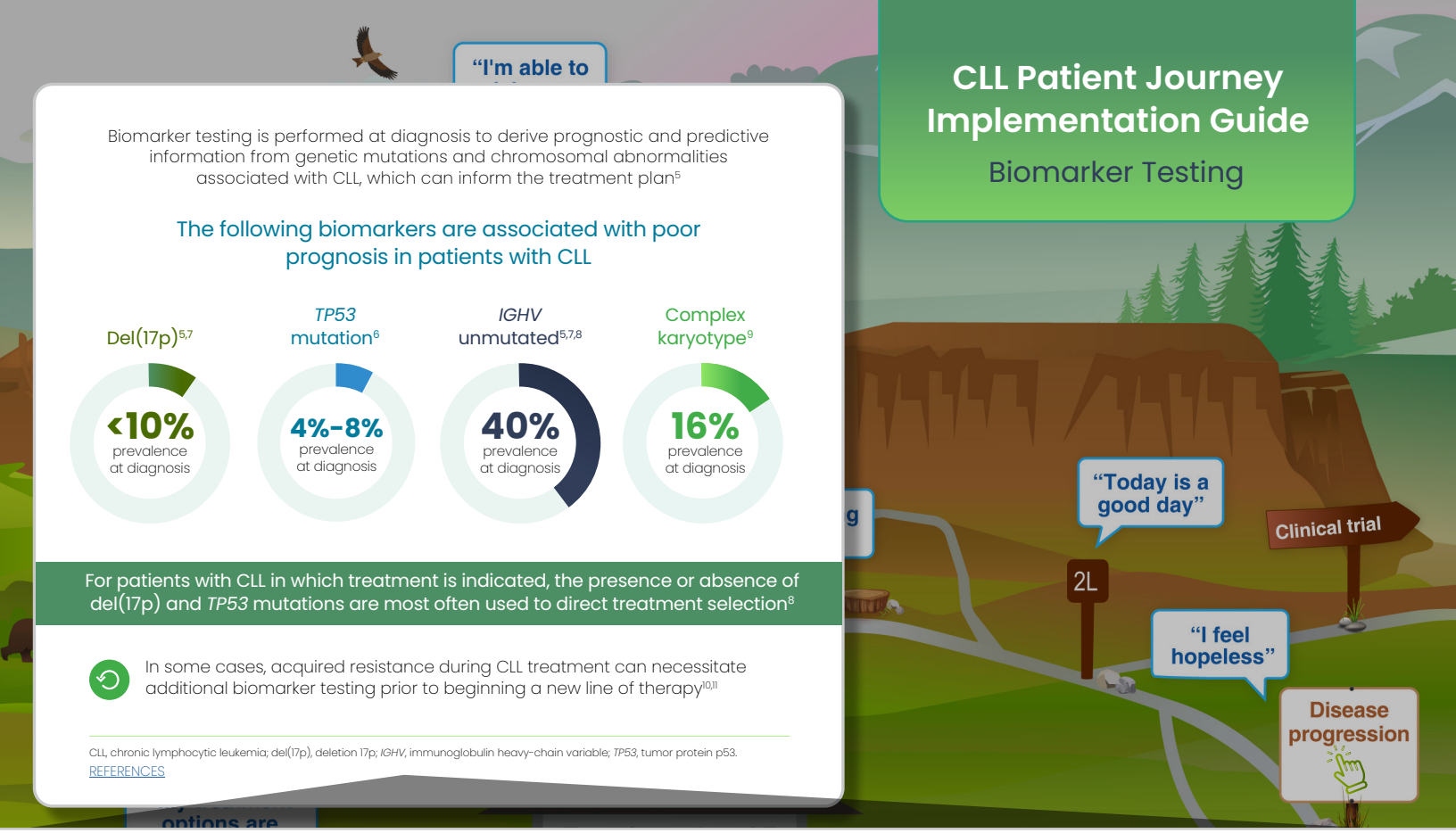

## Objective

- Provide an overview of CLL staging

- After receiving a diagnosis of CLL, the patient will go through disease staging (depicted here as a bridge crossing over a pond) to determine extent of disease
- Several factors weigh into how a patient with CLL is staged including risk of progression, presence of lymphocytosis, degree of lymph node, spleen, and liver enlargement as well as presence of anemia and thrombocytopenia
- The most commonly used CLL staging systems are Rai, Binet, and CLL-IPI
- Once the patient's CLL has been staged, the next stop on the path is biomarker testing to help determine disease prognosis and any relevant predictive information

## Key Talking Points

- Educate the patient on why CLL 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 CLL journey

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## Objective

- Provide an overview of CLL biomarker testing

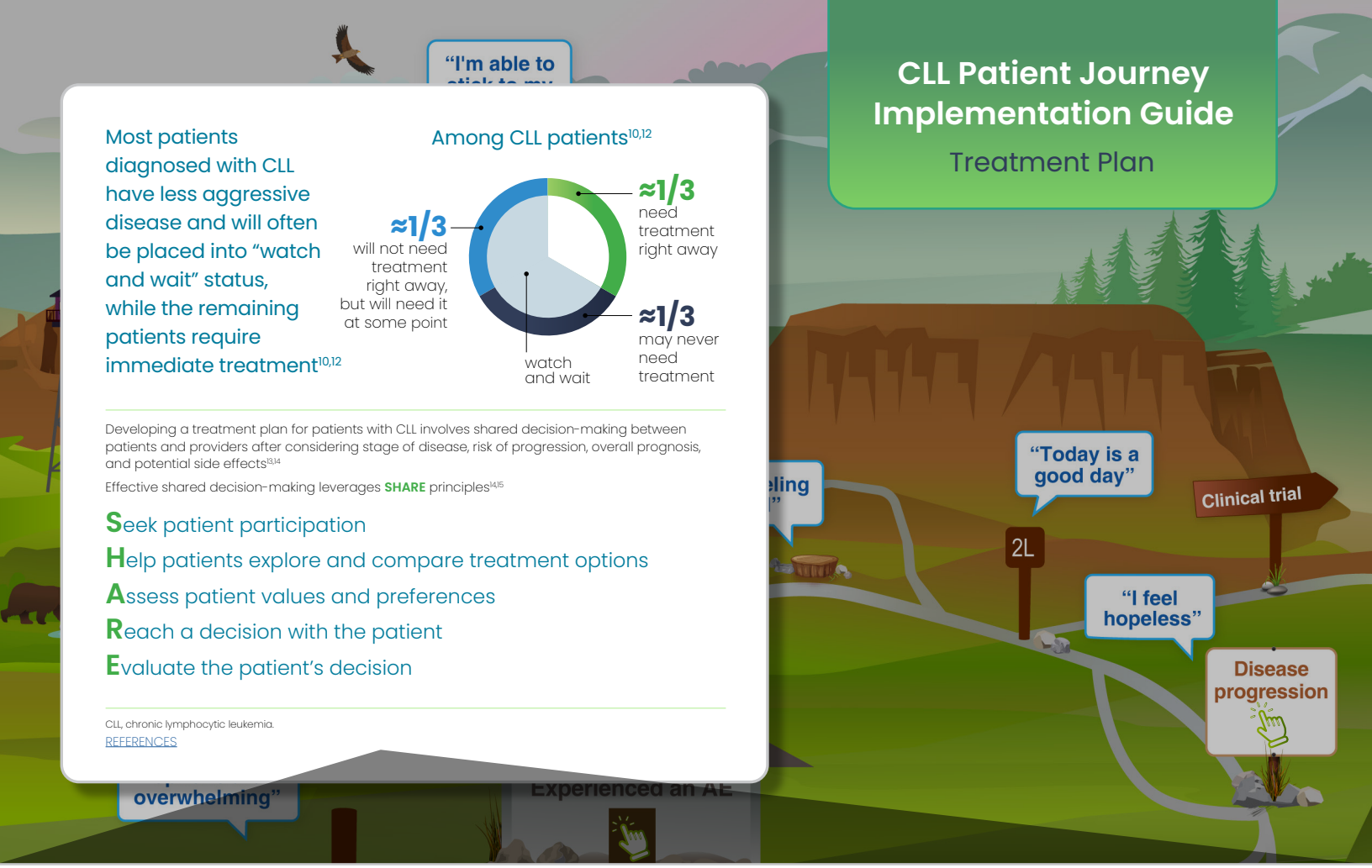
- After CLL staging, the patient will undergo biomarker testing (shown as a fishing platform on the bridge) to help determine disease prognosis and any relevant predictive information
- Biomarker testing involves looking for the presence of genetic mutations and chromosomal abnormalities that are predictive of high-risk disease and/or poor prognosis
- In addition to helping the patient and their HCP understand overall disease outlook, the results of biomarker testing are often used to guide treatment selection
- Additional biomarker testing may also occur at a later stage of the journey to determine if patients have developed acquired resistance mutations to treatment or developed other genetic alterations at each disease progression (denoted as a boat with the ability to take a water path down to the biomarker testing pier)
- Once the patient has undergone initial biomarker testing, the next step of the journey is developing a treatment plan

## Key Talking Points

- Educate the patient on why biomarker testing is performed, enabling the HCP-patient team to have all necessary information before deciding on a treatment path forward
- Review common biomarkers, associated data, and prognostic implications
- Discuss which biomarker(s) the patient has been tested for (if testing has already been completed) or provide next steps for the patient to get tested
- Share that additional biomarker testing may be required at a later time to ensure patients have not developed resistance to certain treatment classes or developed other genetic alterations not present at diagnosis
- Review next steps on the patient's CLL journey

# CLL Patient Journey Implementation Guide

## Treatment Plan

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## Objective

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

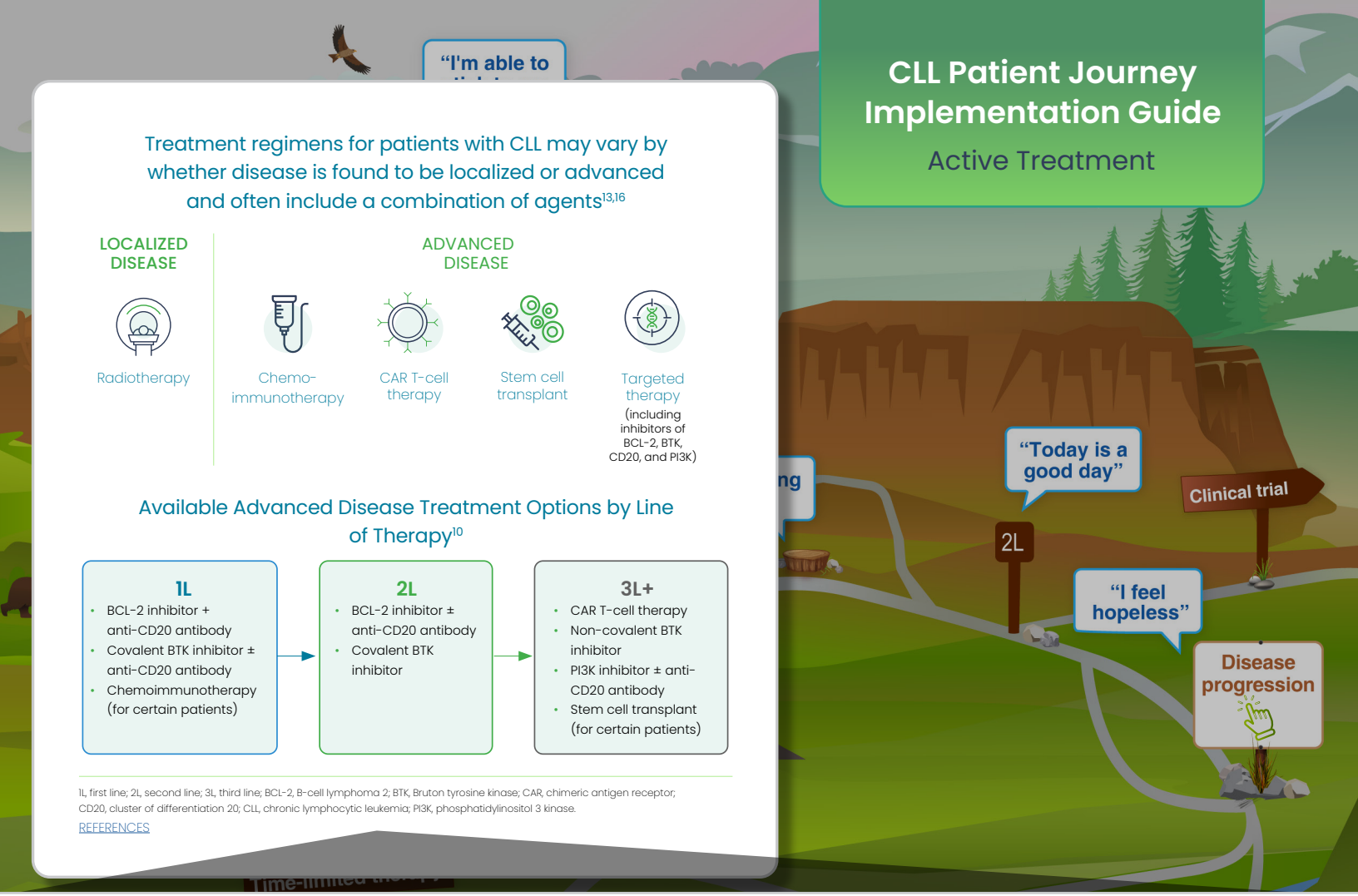
- Once the patient and their HCP have a good understanding of disease prognosis, the CLL journey continues with the development of a treatment plan
- Developing a treatment plan involves shared decision-making between the patient and their HCP, ensuring patient preferences are considered throughout the process
- Two options exist for the next portion of the CLL journey, shown here as a forked path, where two thirds of patients diagnosed with CLL will be placed into "watch and wait" status (depicted here as an inn), which is a period of expectant monitoring where there is no treatment but the patient is routinely assessed, while another third of patients require active treatment (displayed as a trailhead)
- Some 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 "watch and wait" (a period of active surveillance, where there is no treatment but the patient is routinely assessed) vs "active treatment" status
- 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 CLL journey

# CLL Patient Journey Implementation Guide

## Active Treatment




Treatment regimens for patients with CLL may vary by whether disease is found to be localized or advanced and often include a combination of agents[13,16]

**LOCALIZED DISEASE**

- Radiotherapy

**ADVANCED DISEASE**

- Chemo-immunotherapy
- CAR T-cell therapy
- Stem cell transplant
- Targeted therapy (including inhibitors of BCL-2, BTK, CD20, and PI3K)

### Available Advanced Disease Treatment Options by Line of Therapy[10]

**1L**
- BCL-2 inhibitor + anti-CD20 antibody
- Covalent BTK inhibitor ± anti-CD20 antibody
- Chemoimmunotherapy (for certain patients)

→

**2L**
- BCL-2 inhibitor ± anti-CD20 antibody
- Covalent BTK inhibitor

→

**3L+**
- CAR T-cell therapy
- Non-covalent BTK inhibitor
- PI3K inhibitor ± anti-CD20 antibody
- Stem cell transplant (for certain patients)

1L, first line; 2L, second line; 3L, third line; BCL-2, B-cell lymphoma 2; BTK, Bruton tyrosine kinase; CAR, chimeric antigen receptor; CD20, cluster of differentiation 20; CLL, chronic lymphocytic leukemia; PI3K, phosphatidylinositol 3 kinase.

REFERENCES

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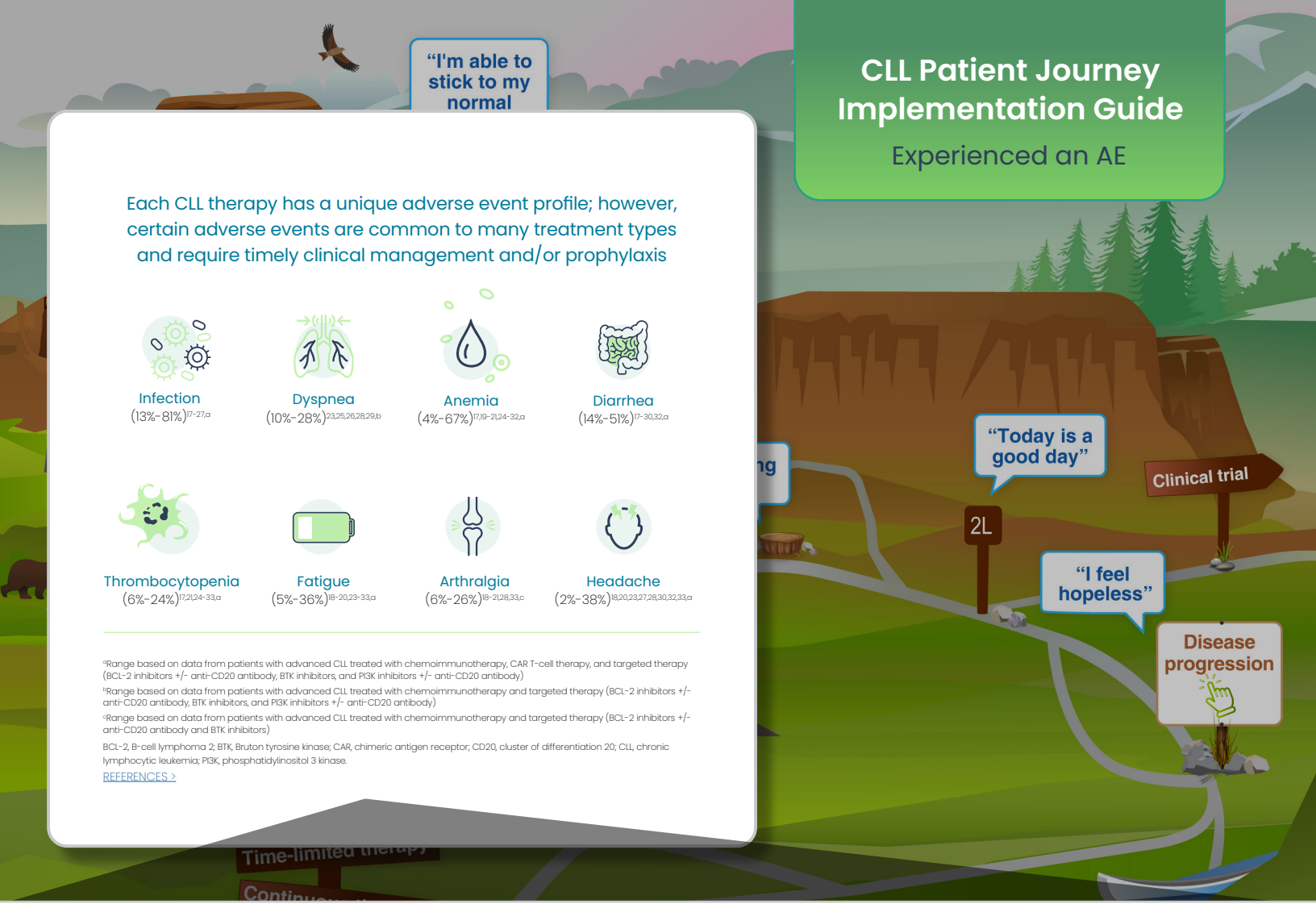
## Objective

- 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 staging, disease severity, biomarker testing, as well as patient and HCP shared decision-making
- The number of treatment options can be overwhelming for patients (indicated here by a quote, "my treatment options are overwhelming"), especially options for those with advanced disease (eg, chemoimmunotherapy, CAR T-cell therapy, stem cell transplant, and targeted therapy [including BCL-2, BTK, CD20, and PI3K inhibitors])
- Further, some patients with CLL will receive therapy over a time-limited or fixed duration, while others will receive continuous or prolonged therapy (depicted here as part of the trailhead description)
- 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 will likely 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 CLL 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 CLL journey




# CLL Patient Journey Implementation Guide

## Experienced an AE

Each CLL 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

| | | | |
|---|---|---|---|
| Infection (13%-81%)[7-27,a] | Dyspnea (10%-28%)[23,25,26,28,29,b] | Anemia (4%-67%)[17,19-21,24-32,a] | Diarrhea (14%-51%)[17-30,32,a] |
| Thrombocytopenia (6%-24%)[17,21,24-33,a] | Fatigue (5%-36%)[18-20,23-33,a] | Arthralgia (6%-26%)[18-21,28,33,c] | Headache (2%-38%)[18,20,23,27,28,30,32,33,a] |

[a]Range based on data from patients with advanced CLL treated with chemoimmunotherapy, CAR T-cell therapy, and targeted therapy (BCL-2 inhibitors +/- anti-CD20 antibody, BTK inhibitors, and PI3K inhibitors +/- anti-CD20 antibody)

[b]Range based on data from patients with advanced CLL treated with chemoimmunotherapy and targeted therapy (BCL-2 inhibitors +/- anti-CD20 antibody, BTK inhibitors, and PI3K inhibitors +/- anti-CD20 antibody)

[c]Range based on data from patients with advanced CLL treated with chemoimmunotherapy and targeted therapy (BCL-2 inhibitors +/- anti-CD20 antibody and BTK inhibitors)

BCL-2, B-cell lymphoma 2; BTK, Bruton tyrosine kinase; CAR, chimeric antigen receptor; CD20, cluster of differentiation 20; CLL, chronic lymphocytic leukemia; PI3K, phosphatidylinositol 3 kinase.

REFERENCES >

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## Objective

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

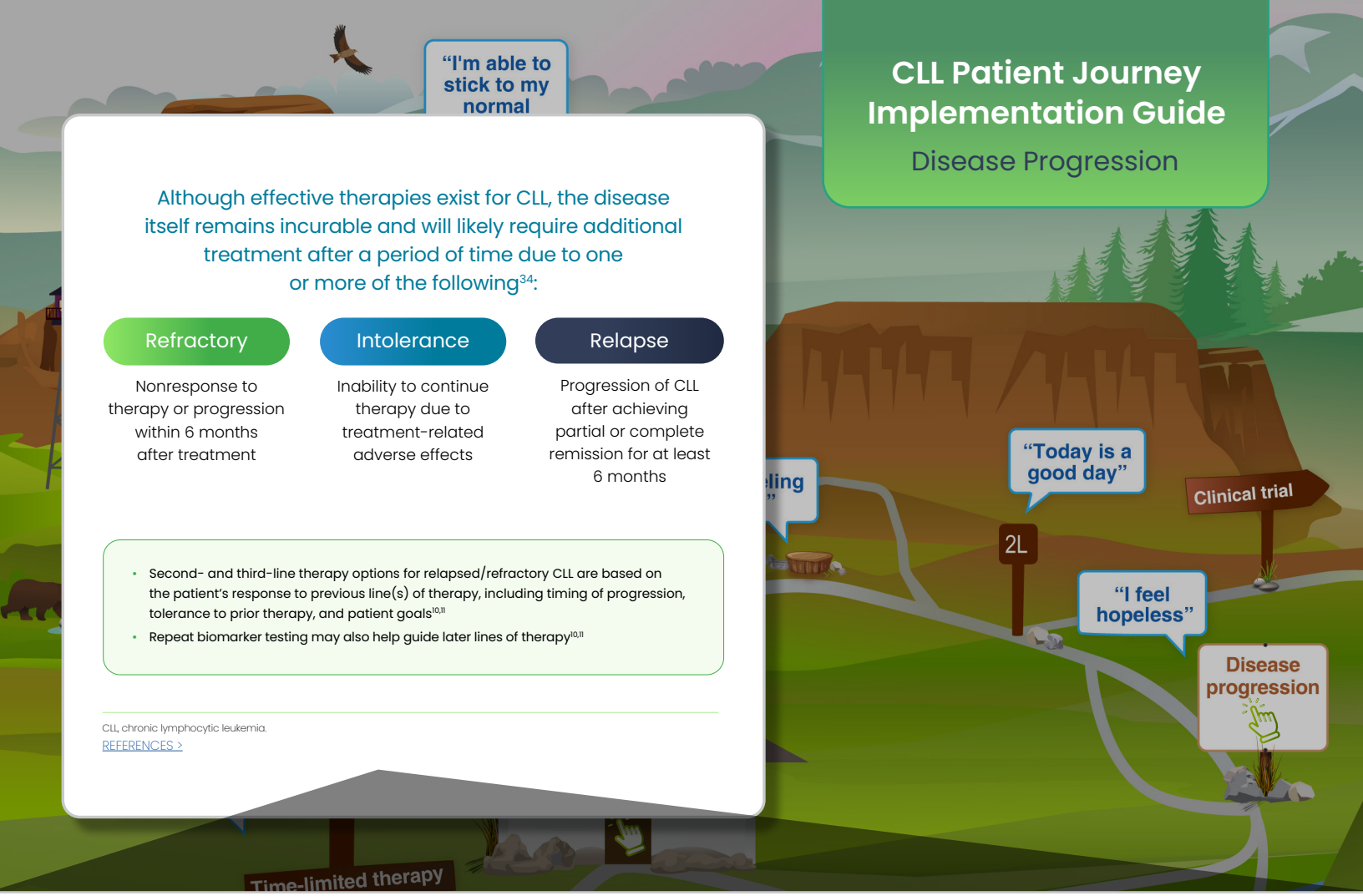
- During active treatment, regardless of line of therapy, a patient may experience adverse events (depicted here as a first-aid station on a side path detour from the main path) that require additional management, dosage modification, and/or discontinuation of therapy
- Common adverse events associated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

## Key Talking Points

- Educate the patient on adverse events associated with CLL treatments, while reiterating that each CLL 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 CLL journey

# CLL Patient Journey Implementation Guide

## Disease Progression




Although effective therapies exist for CLL, the disease itself remains incurable and will likely require additional treatment after a period of time due to one or more of the following[3,4]:

**Refractory**
Nonresponse to therapy or progression within 6 months after treatment

**Intolerance**
Inability to continue therapy due to treatment-related adverse effects

**Relapse**
Progression of CLL after achieving partial or complete remission for at least 6 months

- Second- and third-line therapy options for relapsed/refractory CLL are based on the patient's response to previous line(s) of therapy, including timing of progression, tolerance to prior therapy, and patient goals[10,11]
- Repeat biomarker testing may also help guide later lines of therapy[10,11]

CLL, chronic lymphocytic leukemia.

REFERENCES >

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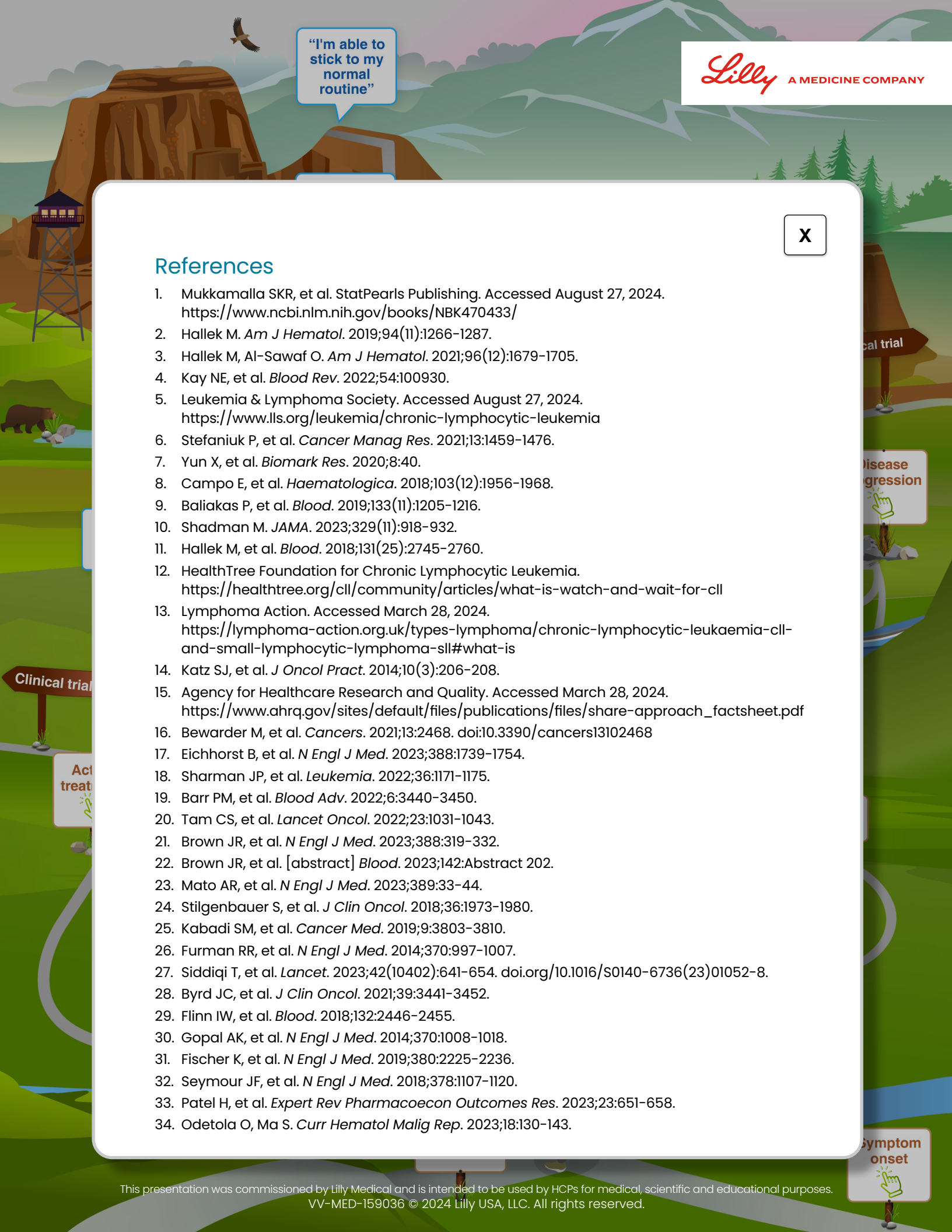
## Objective

- Discuss the causes of CLL disease progression

- Ultimately, a patient with CLL 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)
- A patient with CLL may progress on active treatment due to one or more of the following reasons: nonresponse to therapy (refractory), inability to tolerate treatment-related adverse events (intolerance), or disease progression after initially achieving partial or complete remission (relapse)
- During this time, patients may be feeling uneasy about the outcome of future treatment options. (Denoted by a quote bubble that says, "I feel hopeless.")
- To help guide treatment selection for later lines of therapy, additional biomarker testing may be conducted (shown here as a boat leading back to the main biomarker testing platform)
- For the remainder of the journey, the patient continues to have additional treatment options (as outlined in the active treatment section), 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 CLL disease progression and set expectations for the patient in terms of overall disease outlook
- Share the common causes of disease progression, as well as how these different types differentially impact the next steps of their journey
- Discuss where the patient is in their journey, whether additional biomarker testing is needed, and what next steps are in terms of deciding on a revised treatment plan

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