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

The majority of patients with CLL are asymptomatic and learn of their diagnosis through elevated white blood cell counts during routine blood testing for an unrelated reason[1]

5%–10% will present with symptoms such as[1]:

B symptoms

- Unexplained fevers (>100.5°F)
- Unintentional weight loss (≥10% over 6 months or less)
- Night sweats
- Early satiety
- Fatigue

Other symptoms of CLL

- Swollen lymph nodes
- Increased frequency of infections
- Autoimmune cytopenia
- Enlarged liver or spleen

CLL, chronic lymphocytic leukemia.

REFERENCES >

Abnormal labs

Symptom onset

Patients undergo a variety of tests during initial clinical evaluation once symptoms are evident or an abnormal finding on a routine blood test has occurred[2-5]

History and physical examination

- Patient history to look for signs and symptoms of lymphoma
- Physical examination with specific evaluation of the lymph nodes
- Performance status
- May include imaging of liver, spleen, and lymph nodes

Immunophenotyping

- Measures cell number and characteristics to compare cancer cells to normal cells
- Determines if abnormal lymphocytes are developed from a single cancer cell or are the result of other noncancerous conditions

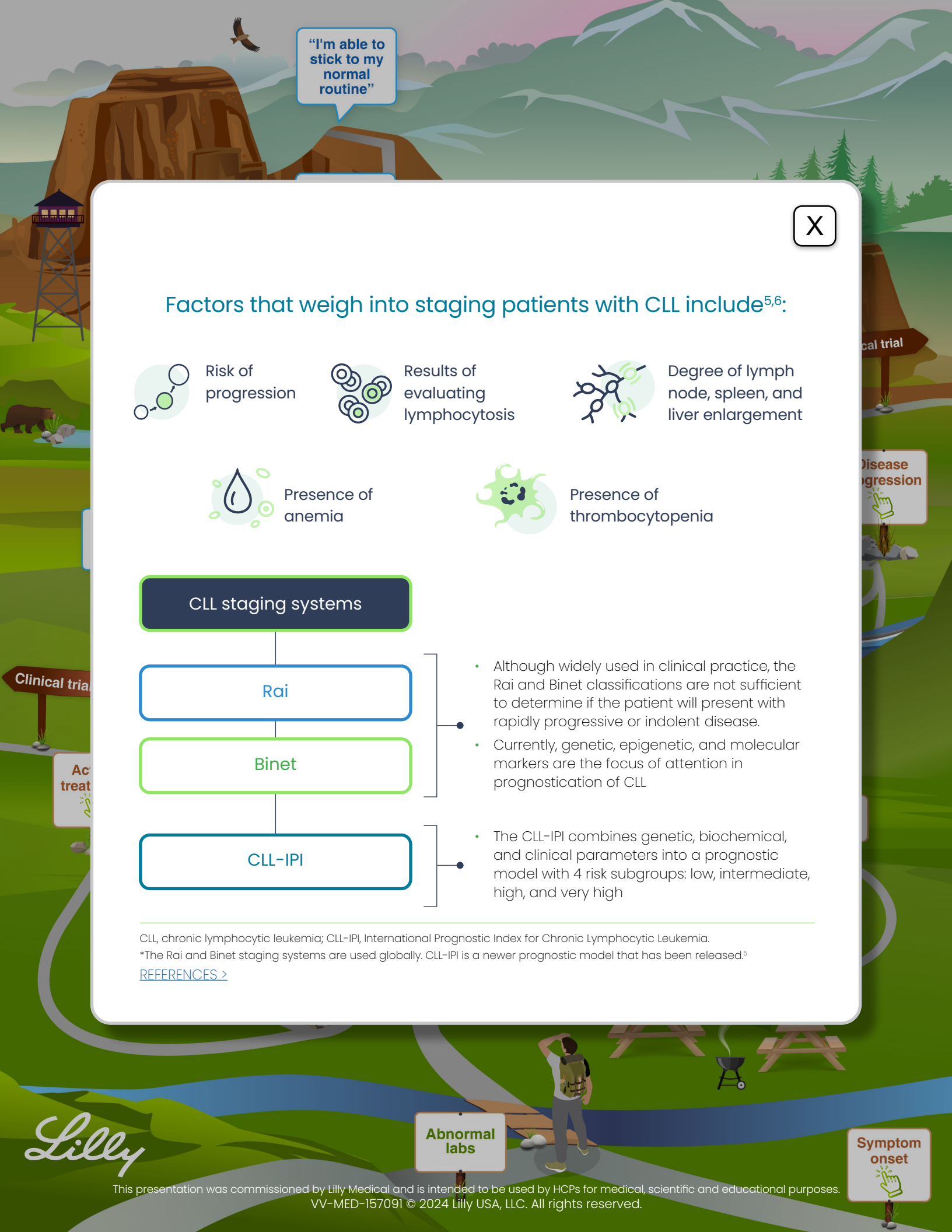
Laboratory testing

- Complete blood count
- Comprehensive metabolic panel

Histopathology

- Review of blood smear and/or bone marrow biopsy

REFERENCES >



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Factors that weigh into staging patients with CLL include[5,6]:

- Risk of progression
- Results of evaluating lymphocytosis
- Degree of lymph node, spleen, and liver enlargement
- Presence of anemia
- Presence of thrombocytopenia

CLL staging systems

Rai

Binet

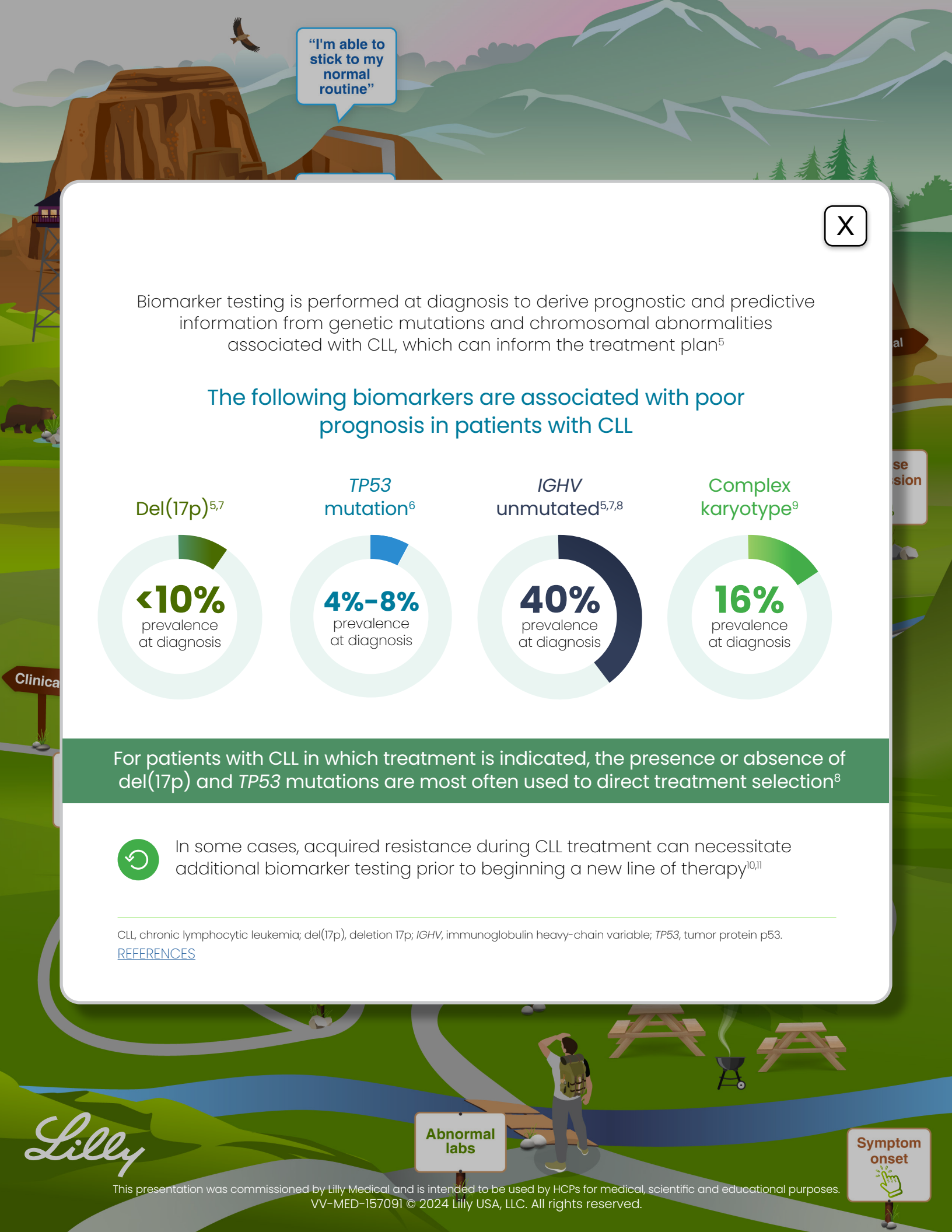
- Although widely used in clinical practice, the Rai and Binet classifications are not sufficient to determine if the patient will present with rapidly progressive or indolent disease.
- Currently, genetic, epigenetic, and molecular markers are the focus of attention in prognostication of CLL

CLL-IPI

- The CLL-IPI combines genetic, biochemical, and clinical parameters into a prognostic model with 4 risk subgroups: low, intermediate, high, and very high

CLL, chronic lymphocytic leukemia; CLL-IPI, International Prognostic Index for Chronic Lymphocytic Leukemia.
*The Rai and Binet staging systems are used globally. CLL-IPI is a newer prognostic model that has been released.[5]

REFERENCES >



Biomarker testing is performed at diagnosis to derive prognostic and predictive information from genetic mutations and chromosomal abnormalities associated with CLL, which can inform the treatment plan[5]

The following biomarkers are associated with poor prognosis in patients with CLL

Del(17p)[5,7]

<10%
prevalence at diagnosis

TP53 mutation[6]

4%–8%
prevalence at diagnosis

IGHV unmutated[5,7,8]

40%
prevalence at diagnosis

Complex karyotype[9]

16%
prevalence at diagnosis

For patients with CLL in which treatment is indicated, the presence or absence of del(17p) and *TP53* mutations are most often used to direct treatment selection[8]

In some cases, acquired resistance during CLL treatment can necessitate additional biomarker testing prior to beginning a new line of therapy[10,11]

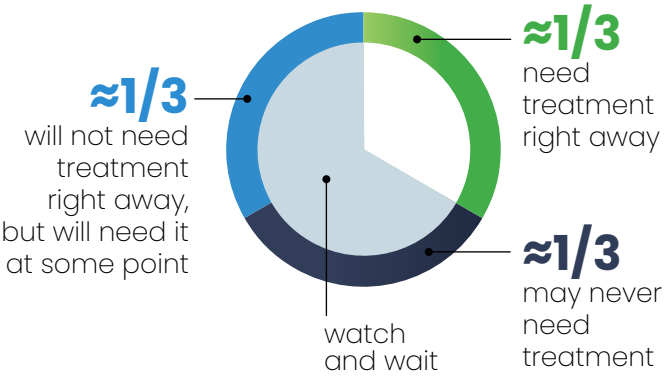
CLL, chronic lymphocytic leukemia; del(17p), deletion 17p; *IGHV*, immunoglobulin heavy-chain variable; *TP53*, tumor protein p53.

REFERENCES

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

Most patients diagnosed with CLL have less aggressive disease and will often be placed into "watch and wait" status, while the remaining patients require immediate treatment[10,12]

Among CLL patients[10,12]



Developing a treatment plan for patients with CLL involves shared decision-making between patients and providers after considering stage of disease, risk of progression, overall prognosis, and potential side effects[13,14]

Effective shared decision-making leverages **SHARE** principles[14,15]

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

CLL, chronic lymphocytic leukemia.

REFERENCES

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

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

Clinical

Abnormal labs

Symptom onset

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

Abnormal labs

Symptom onset

X

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%)[17-27,a]

Dyspnea
(10%-28%)[23,25,26,28,29,b]

Anemia
(5%-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]

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[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.

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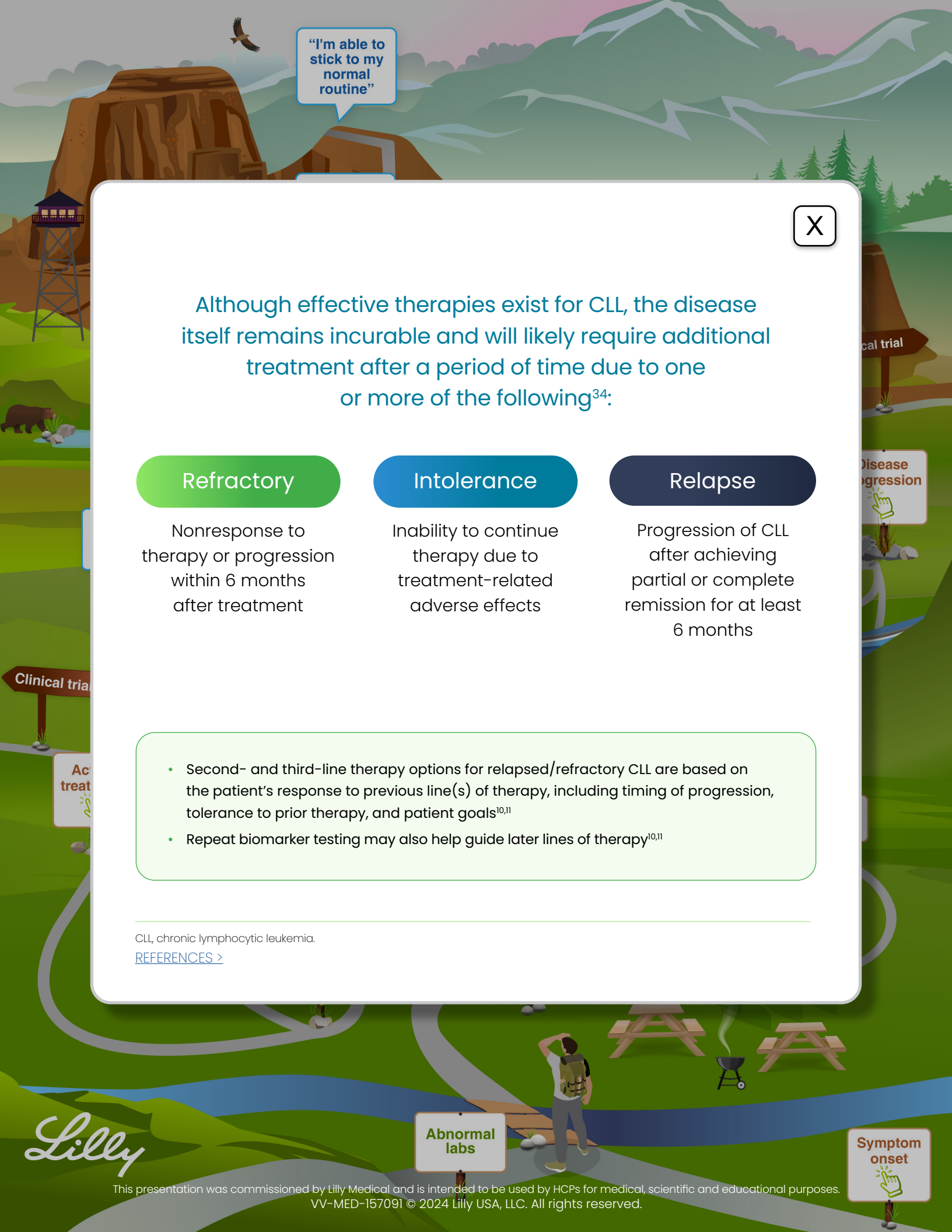

Although effective therapies exist for CLL, the disease itself remains incurable and will likely require additional treatment after a period of time due to one or more of the following[34]:

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.

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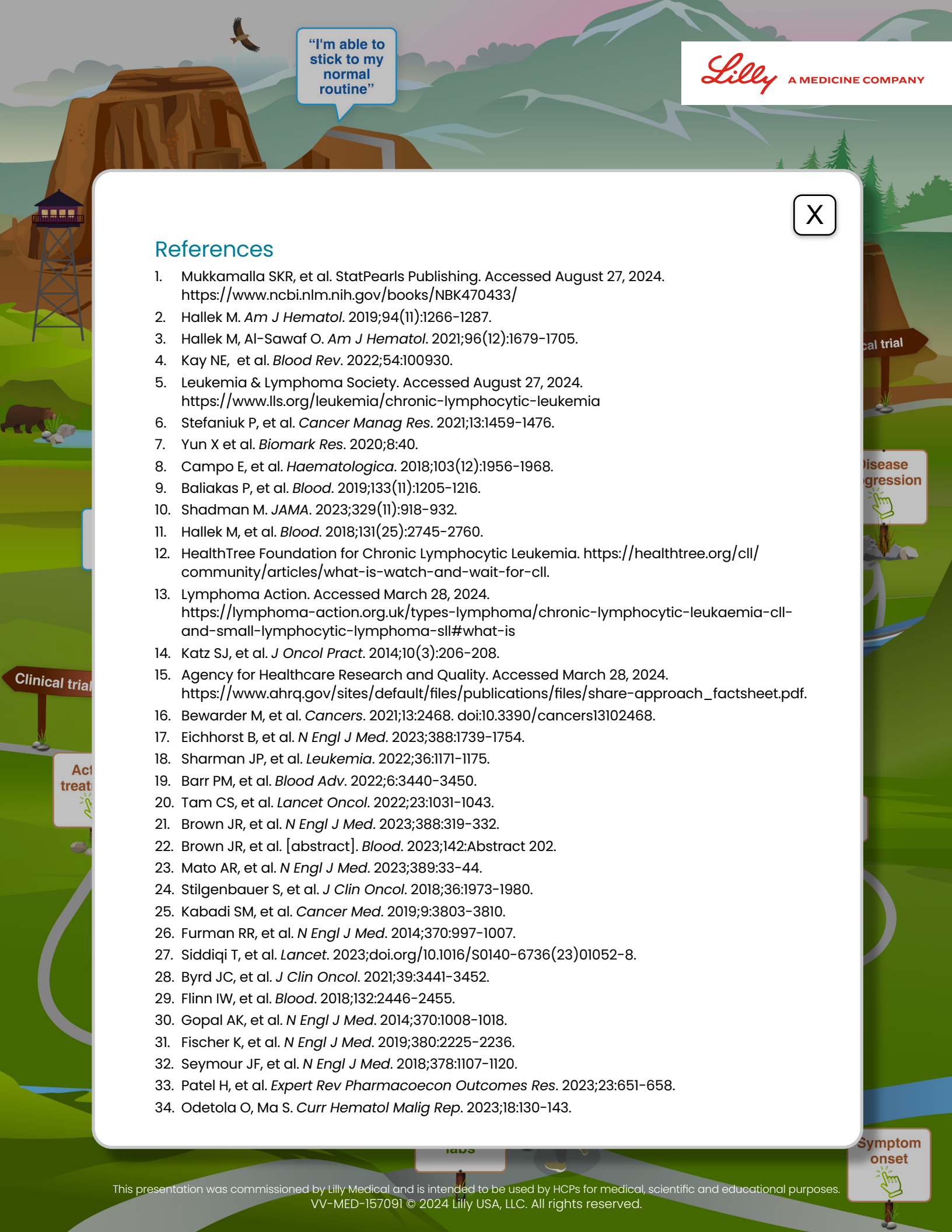

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