CLL Patient Journey Patient Case

Introduction and Instructions

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

"I am afraid to switch

X

Objective

- This hypothetical patient case is intended to illustrate the CLL patient journey through a step-by-step process from medical history and initial presentation to on-label selection of CLL treatment

Key Talking Points

- The CLL patient case is intended as a tool for HCPs to use when communicating with patients. Provided within the format of the original patient journey map, this tool brings the case to life in an easily relatable way that can be shared with patients during their journey through CLL diagnosis and treatment.

Introduction

Meet Robert, a 71-year old Caucasian male patient. From his medical history, we can see Robert generally takes good care of himself but does face challenges with diabetes and heart health.

Social History

- Occupation – retired factory worker
- Smoking status – never
- Alcohol use – rare
- Exercise – walks in a local park 1-2 times per week

Medical history/comorbidities

- Type 2 diabetes
- Hypercholesterolemia
- Arterial stent placement

Current medications/supplements

- Metformin
- Atorvastatin
- Low-dose aspirin
- Calcium
- Famotidine

CLL Patient Journey
Patient Case
Symptom Onset

"I'm able to stick to my normal

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 >

"Today is a good day"

2L

Clinical trial

"I feel hopeless"

Disease progression

Symptom Onset

X

Robert reported to his primary care doctor for his annual physical exam and bloodwork where he learned that his white blood cell count was elevated. Given these test results, Robert's primary care doctor decided to order additional testing to determine a possible cause for his elevated white blood cell count.

CLL Patient Journey
Patient Case
Clinical Evaluation

"I'm able to stick to my normal

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 >

"I'm feeling tired"

"Today is a good day"

2L

Clinical trial

"I feel hopeless"

Disease progression

"My treatment options are overwhelming"

Experienced an AE

Clinical Evaluation

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- Robert was referred to a hematologic oncologist where he received a physical exam, and the oncologist collected his medical history. He also underwent additional laboratory testing
- Robert's physical exam showed that the lymph nodes in his neck and underarm regions were enlarged. He also had elevated levels of lymphocytes in his blood. Additional testing, such as immunophenotyping and histopathology, was performed to look at blood and bone marrow samples under a microscope

Physical exam:
enlarged axillary and cervical lymph nodes

Lymphocyte count:
51,210/µL

Platelet count:
185,000/µL

Histopathology:
55%
lymphocytic dominance

Immunophenotyping:
flow cytometry level of
6,500/µL
and non-complex karyotype

CLL Patient Journey
Patient Case
Staging

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

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 >

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Staging

- The test results from Robert's initial visit with the hematologic oncologist were definitive enough to diagnose him with chronic lymphocytic leukemia
- Robert's HCP also wanted to determine the extent of his disease by staging him with the Rai staging criteria
- Considering his previous exam and test results, Robert's HCP determined that he had stage I CLL

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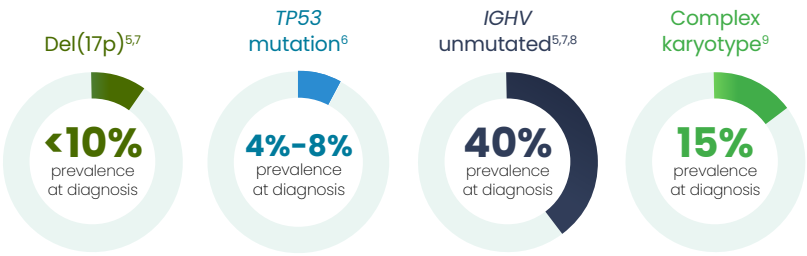
- Enlarged lymph nodes
- Lymphocyte count >5 × 10^9/L
- Bone marrow lymphocytes >40%

→ Rai Stage I CLL

CLL Patient Journey
Patient Case
Biomarker Testing

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



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

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options are overwhelming"
Experienced an AE

Biomarker Testing

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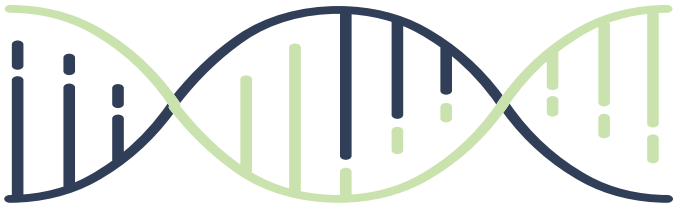
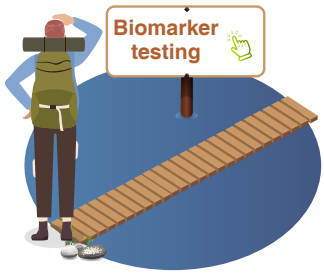
- Robert's HCP also ordered biomarker testing so he could determine Robert's disease prognosis and the likelihood of response to certain therapies based on the presence of genetic mutations
- Robert was positive for *IGHV* mutation and negative for all other biomarkers (including del(17p) and *TP53* mutation), indicative of a better overall prognosis



Biomarker Summary

- *IGHV*-mutated
- Negative for del(17p), *TP53* mutation, and complex karyotype



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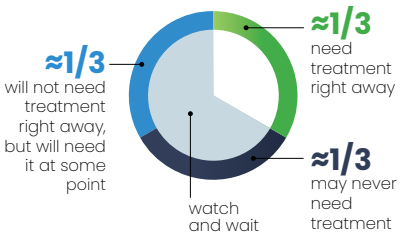
Treatment Plan

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

CL, chronic lymphocytic leukemia.

REFERENCES

"I'm able to

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Disease progression

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Experienced an AE

Treatment Plan

- Given the lack of symptoms and a better overall prognosis, Robert and his provider agreed (via a shared decision-making process) to move forward with "watch and wait" status where he would not receive treatment at this time
- Robert was also comfortable with regular outpatient follow-up every 3 months

CLL Patient Journey
Patient Case
Active Treatment

"I'm able to stick to my

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.

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Disease progression

Active Treatment

- After 2 years of "watch and wait", Robert begins to experience more symptoms which trigger the need for additional laboratory and molecular testing to determine how the disease is progressing
- Robert's test results indicated that he needed to be placed on active treatment and he and his HCP decided to move forward with ibrutinib* (an orally-administered covalent BTK inhibitor) as first-line treatment

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*Imbruvica Prescribing Information: https://www.rxabbvie.com/pdf/imbruvica_pi.pdf.

CLL Patient Journey
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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%)[17-26,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%)[18-21,27,33,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.

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Experienced an AE

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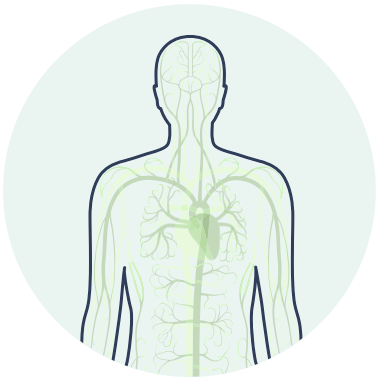
- Potentially impacted by his heart health issues, Robert experienced a cardiac toxicity (grade 3 hypertension) after 4 months of partial response to ibrutinib*



Hypertension

*Imbruvica Prescribing Information: https://www.rxabbvie.com/pdf/imbruvica_pi.pdf.

CLL Patient Journey
Patient Case
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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Therapy Intolerance

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- The cardiac toxicity (grade 3 hypertension) Robert experienced after 4 months of partial response required him to discontinue taking ibrutinib* therapy
- Since Robert did initially respond to ibrutinib and had to discontinue due to intolerance rather than his disease progressing, he and his HCP mutually decided to try alternative first-line therapy with zanubrutinib† (another orally-administered covalent BTK inhibitor)

"Let's try zanubrutinib as an alternative first-line therapy"

*Imbruvica Prescribing Information: https://www.rxabbvie.com/pdf/imbruvica_pi.pdf.
†Brukinsa Prescribing Information: https://d1e94vsyskgtht.cloudfront.net/brukinsa/pdfs/brukinsa-prescribing-information.pdf.

CLL Patient Journey
Patient Case

2L

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Disease progression

Disease Progression and 2L Therapy

- For 2 years, Robert partially responded to zanubrutinib and experienced a grade 1 upper respiratory tract infection and grade 2 arthralgia
- Eventually, Robert progressed on zanubrutinib* and his HCP ordered additional biomarker testing to determine if a genetic mutation had developed to make him resistant to treatment
- Robert's biomarker test results showed that he did develop a mutation that made him resistant to treatments like zanubrutinib, requiring him to move on to second-line therapy with venetoclax† (a BCL-2 inhibitor) and rituximab‡ (an anti-CD20 antibody)

*Brukinsa Prescribing Information: https://d1e94vsyskgtht.cloudfront.net/brukinsa/pdfs/brukinsa-prescribing-information.pdf. †Venclexta Prescribing Information: https://www.rxabbvie.com/pdf/venclexta.pdf. ‡Rituxan Prescribing Information: https://www.gene.com/download/pdf/rituxan_prescribing.pdf.

CLL Patient Journey
Patient Case

3L

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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

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- Repeat biomarker testing may also help guide later lines of therapy[10,11]

CLL, chronic lymphocytic leukemia.

REFERENCES >

3L Therapy

- Unfortunately, Robert progressed on venetoclax* + rituximab† therapy after 1 year of treatment, likely due to CLL disease evolution, his advanced age, his other health issues, and several years of prior CLL treatment
- Aligning with patient goals of care, Robert and his HCP decided to move forward with pirtobrutinib,‡ an orally-administered noncovalent BTK inhibitor that can still be used after intolerance to or progression on a covalent BTKi to continue to leverage the potential clinical benefits of blocking the BTK pathway
- Currently, Robert has been receiving pirtobrutinib for 6 months and is partially responding to treatment; during that time, he has experienced grade 1 fatigue and grade 2 arthralgia
- Because CLL remains incurable, Robert will likely relapse after a period of time, requiring entry into a clinical trial or treatment with other recommended therapies

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"Pirtobrutinib is a noncovalent BTK inhibitor that can still be used despite intolerance to or progression on a covalent BTK inhibitor like ibrutinib"

*Venclexta Prescribing Information: https://www.rxabbvie.com/pdf/venclexta.pdf.
†Rituxan Prescribing Information: https://www.gene.com/download/pdf/rituxan_prescribing.pdf. ‡Pirtobrutinib Prescribing Information: https://uspl.lilly.com/jaypirca/jaypirca.html?s=pi.