



Clinical course of chronic lymphocytic leukaemia (CLL)

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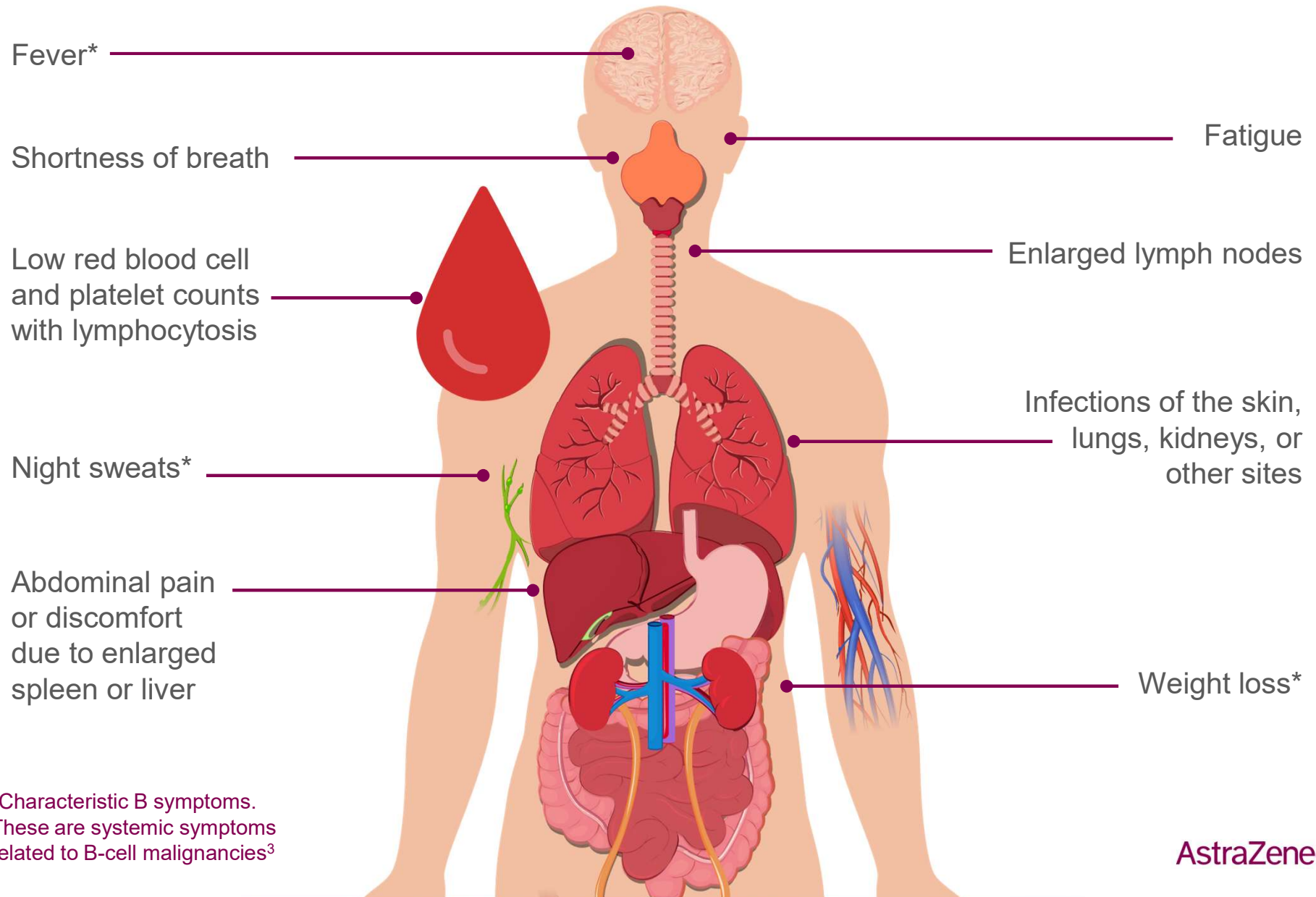
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Signs and symptoms of CLL

Signs and symptoms of CLL

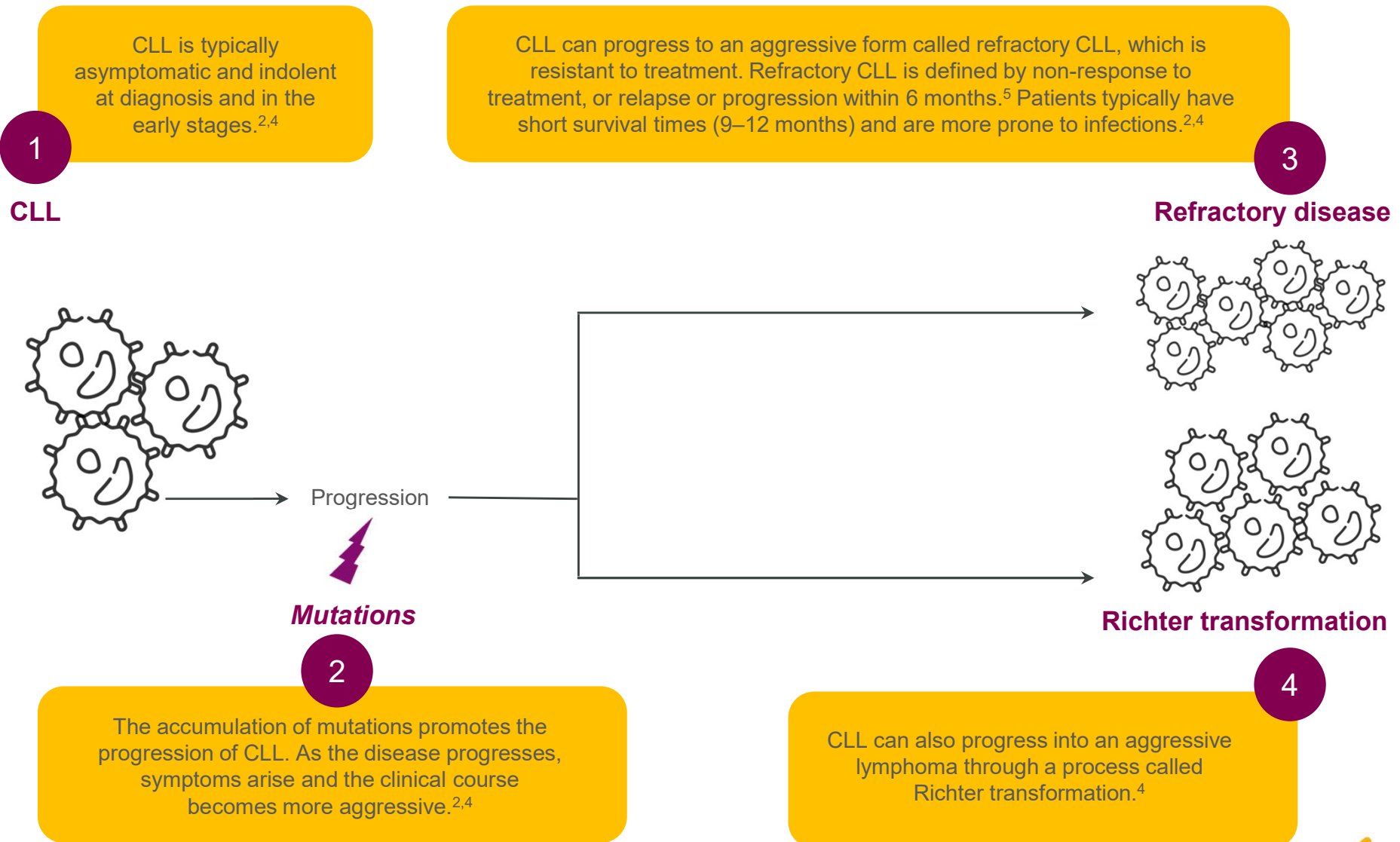
- Most patients with **CLL** do not present with any symptoms at diagnosis.
- When present, **B symptoms** and **symptoms specific to CLL** may include:^{1,2}



Progression of CLL

Progression of CLL

The **clinical manifestations** of CLL typically intensify with disease progression.²
The **clinical course** also becomes more aggressive.⁴



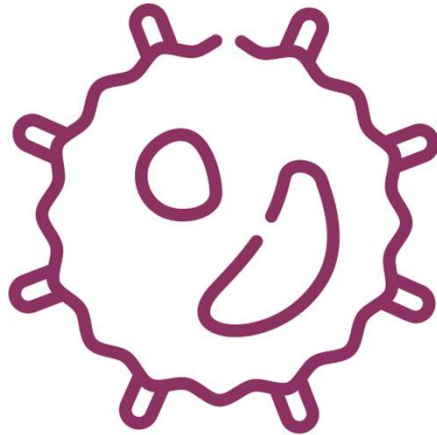
Richter transformation

Definition of Richter transformation

Richter transformation involves the progression of CLL to an **aggressive form of lymphoma**⁴

Diffuse large B-cell lymphoma (DLBCL)

DLBCL is the most common⁴. It is a type of non-Hodgkin lymphoma characterised by a rapidly growing tumour. This can spread diffusely to the lymph nodes, spleen, liver, or bone marrow⁶



Hodgkin lymphoma

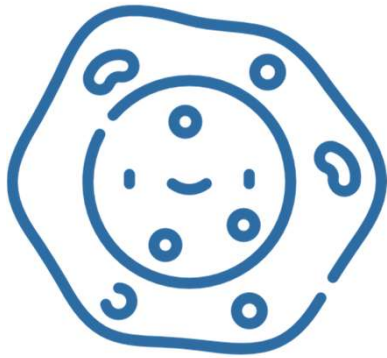
CLL can also transform into Hodgkin lymphoma. This is characterised by the presence of a large, abnormal lymphocyte called the Reed-Sternberg cell^{4,6}

Incidence of Richter transformation⁷

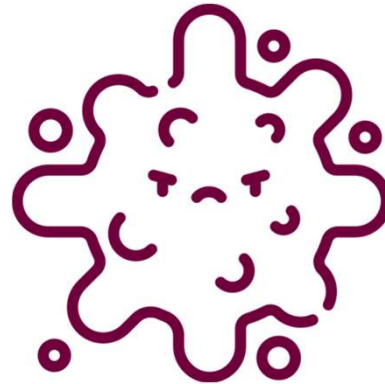


Mechanism of Richter transformation

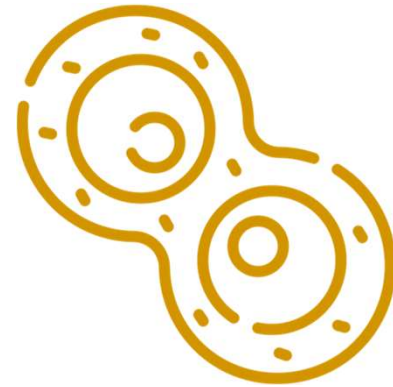
Richter transformation is the result of an **accumulation of mutations that dysregulate**:⁴



Tumour suppressors



Cell proliferation



Cell cycle control

The **TP53** tumour suppressor gene is involved in **50-60% of cases**, and the activation of aberrations of **NOTCH1** and MYC pathways in about **30% of cases**.⁸

Symptoms of Richter transformation

Richter transformation is characterised by **rapidly progressive lymph node disease** and the following **B symptoms**:²

Fever

Night sweats

Weight loss



Watch this video
from **Dr Toby Eyre** on the
management of **Richter**
transformation

Summary

Summary



Signs and symptoms

- Most people with CLL do not present with any symptoms at diagnosis
- When present, symptoms may include:
 - lymphocytosis
 - shortness of breath
 - fatigue
 - low red blood cell and platelet counts
 - enlarged lymph nodes, spleen or liver
 - infections of the skin, lungs, kidneys or other sites
 - B symptoms such as fever, night sweats, and weight loss



Progression of CLL

- The clinical manifestations of CLL typically intensify
- The clinical course becomes more aggressive
- CLL can progress to diffuse large B-cell lymphoma (DLBCL) or Hodgkin lymphoma through a process called Richter transformation



Richter transformation

- Richter transformation is characterised by rapidly progressive lymph node disease and certain B symptoms
- Richter transformation is the result of an accumulation of mutations that dysregulate tumour suppressors, cell proliferation and cell cycle control

Knowledge check

Knowledge check: questions

1. True or false: Patients with CLL typically present with symptoms of fatigue, low blood cell counts, and enlarged lymph nodes at diagnosis.

- A. True
- B. False

2. Fill in the blanks: The clinical manifestations of CLL typically _____ with disease progression. The clinical course becomes _____ aggressive as CLL progresses.

- A. decrease, less
- B. decrease, more
- C. increase, less
- D. increase, more

3. Fill in the blanks: Richter transformation involves the progression of _____ to an aggressive form of _____.

- A. AML, CLL
- B. CLL, AML
- C. CLL, lymphoma
- D. Lymphoma, CLL

4. Richter transformation arises from the accumulation of mutations that dysregulate which of the following cellular processes?

- A. Cell cycle control, necrosis, and tumour suppressors
- B. Cell proliferation, differentiation, and apoptosis
- C. Oncogenes, tumour suppressors, and cell survival
- D. Tumour suppressors, cell proliferation, and cell cycle control

Knowledge check: answers

1. **B: False** Most patients with CLL **do not** present with any symptoms at diagnosis.
2. **D:** The clinical manifestations of CLL typically increase with disease progression. The clinical course becomes more aggressive as CLL progresses.
3. **C:** Richter transformation involves the progression of CLL to an aggressive form of lymphoma.
4. **D:** Richter transformation arises from the accumulation of mutations that dysregulate tumour suppressors, cell proliferation, and cell cycle control.

References

References

1. Wierda WG, Byrd JC, Abramson JS, et al. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®). Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma. V.2.2019. National Comprehensive Cancer Network® (NCCN®). October 2018:1-86.
2. Awan FT, Byrd JC. Chronic Lymphocytic Leukemia. In: Hoffman R, Benz EJ Jr., Silberstein LE, et al, eds. *Hematology: Basic Principles and Practice*. 7th ed. Philadelphia, PA: Elsevier, Inc.; 2018:1244-1264.
3. Non-Hodgkin Lymphoma. Atlanta, GA. American Cancer Society (ACS). February 2016:1-75. Available at: [www.https://www.cancer.org/cancer/non-hodgkin-lymphoma.html](https://www.cancer.org/cancer/non-hodgkin-lymphoma.html).
4. Fabbri G, Dalla-Favera R. The molecular pathogenesis of chronic lymphocytic leukaemia. *Nat Rev Cancer*. 2016;16(3):145-162.
5. Smolewski P, Robak T. Current treatment of refractory/relapsed chronic lymphocytic leukemia: a focus on novel drugs. *Acta Haematol* 2021;144:365–379
6. National Cancer Institute (NCI). NCI Dictionary of Cancer Terms. Bethesda, MD: National Institutes of Health (NIH); 2018.
7. Rossi D, Spina V, Gaidano G. Biology and treatment of Richter syndrome. *Blood*. 2018; 131(25):2761-2772.
8. Tadmor T, Levy I. Richter Transformation in Chronic Lymphocytic Leukemia: Update in the Era of Novel Agents. *Cancers* 2021, 13(20), 5141.