

# Chronic Lymphocytic Leukemia

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## What is Chronic Lymphocytic Leukemia (CLL)?

A slow-growing, life-threatening and incurable cancer of older adults, chronic lymphocytic leukemia (CLL) is a type of mature B-cell malignancy, classified by overgrowth of white blood cells, or lymphocytes, in the bone marrow, the spongy tissue inside bones that produces blood cells, and other tissues.<sup>1,2,3</sup> CLL and small lymphocytic lymphoma (SLL) are considered different manifestations of the same disease.<sup>4</sup>

In CLL, one of the potential causes of the over-accumulation of lymphocytes can be attributed to dysregulated cell proliferation: or overgrowth of cells, attributed to increased activation of the B-cell receptor (BCR) signaling pathway, often driven by an over-expression of mediator cells such as Bruton's tyrosine kinase (BTK).<sup>5,6</sup>

## Prevalence & Incidence



CLL is the most common leukemia in adults, accounting for about

**1/4**

of new cases of leukemia in the U.S.<sup>7,8</sup>



The number of people living with CLL in the United States is expected to increase by

**55%**

from 2011 to 2025 due to increased survival<sup>9</sup>



CLL typically affects older white males, with median age at diagnosis of

**70 years<sup>10</sup>**

Due to the chronic and relapse nature of the disease, patients suffer from diminished quality of life<sup>11,12,13,14</sup>

### Risk Factors

There are minimal risk factors for CLL, but known factors include:<sup>15</sup>

- Age
- Exposure to certain chemicals
- Family history
- Gender
- Race/Ethnicity

Genetic factors may also increase the risk of CLL.<sup>16</sup>

### Symptoms

Symptoms can include:<sup>4,5,17,18,19,20</sup>

- Fatigue
- Anemia (decreased red blood cell count)
- Lymph node enlargement
- Thrombocytopenia (decreased platelet count)
- Low-grade fever
- Unexplained weight loss
- Night sweats
- Feeling of fullness (due to an enlarged spleen or liver)
- Infection of skin, lungs, kidneys, or other organs as a result of low immunoglobulin levels and decreased neutrophil counts

## Prognosis

CLL is considered “*chronic*” as this type of leukemia can be **indolent**, or slow growing, where immediate treatment is not always necessary, and patients may remain stable for years.

However, once the disease becomes **aggressive**, immediate treatment is required because of high numbers of leukemic cells in the blood that block normal cell production.<sup>21</sup> There is no cure for CLL, but recent advancements in treatment have improved survival rates.

**In the U.S., there will be an estimated**  
**4,410**  
**deaths due to CLL this year.<sup>7</sup>**

Patient’s genetic profiles can affect the time to initial treatment and prognosis. In the era of chemotherapy-based regimens, patients with del(17p)/TP53mut had the poorest prognosis, followed by patients with del(11q) and unmutated IGHV.<sup>22,23,24,25,26</sup>

## Diagnosis & Treatment

- Unexplained elevated white blood cell (lymphocyte) count is the most common finding leading physicians to consider a diagnosis of CLL.<sup>6,27</sup>
- Abnormal results from blood tests or as part of an annual physical or a medical examination for an unrelated condition. Due to this, many people with CLL are diagnosed before they display symptoms.

**The goal of CLL therapy is to achieve durable remission while maintaining quality of life, by limiting treatment toxicity.<sup>28</sup>**

- Various treatment strategies are available to CLL patients, including “watch and wait.”<sup>25</sup>
- Treatment choice is guided by multiple factors including genetic profile, age, comorbidities, comedications, patient’s preference and potential side effects.
- Current standard of care in the treatment of high-risk frontline and R/R CLL is continuous treatment with BTK inhibitor therapy, however other treatment backbones include time-limited chemoimmunotherapy (CIT), and time-limited venetoclax combinations.
- However, some patients are unable to tolerate or do not respond to currently available therapies, or their disease returns after treatment.<sup>5</sup>
- Adverse events and subsequent treatment discontinuation have a negative impact on patients’ prognosis, underscoring the need for additional treatment options<sup>29-38</sup>

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