

ABOUT PHILADELPHIA CHROMOSOME-POSITIVE ACUTE LYMPHOBLASTIC LEUKEMIA (PH+ ALL)

Acute lymphoblastic leukemia (ALL) results from a mutation in a stem cell in the bone marrow. This mutated cell becomes a leukemic cell and begins multiplying uncontrollably. These early cells are called lymphoblasts, and they block the production of normal, healthy blood cells.¹

There are several subtypes of ALL, including Philadelphia chromosome-positive acute lymphoblastic leukemia (Ph+ ALL).^{1,2}

- **Ph+ ALL is a rare subtype of leukemia** characterized by the abnormal formation of the Philadelphia chromosome, which leads to the development of the BCR::ABL1 gene.²
- **The BCR::ABL1 gene** creates an abnormal protein that allows for leukemia cell growth.²
- Ph+ ALL is a fast progressing and aggressive disease, and the long-term prognosis is poor. **Individuals with Ph+ ALL typically have a worse prognosis than those with other subtypes of ALL.**^{3,4}

Prevalence of Ph+ ALL

In the United States, **over 900 people** are diagnosed with Ph+ ALL each year.⁵

Ph+ ALL accounts for **25% of adults diagnosed with ALL and 1-3% of children diagnosed with ALL.**^{6,7}

Treatment Considerations for Ph+ ALL

There are several factors to consider when choosing a treatment path for Ph+ ALL.^{8,9}

Various tyrosine kinase inhibitors (TKIs), which are oral medications, in combination with chemotherapy, steroids or immunotherapies are often used to treat Ph+ ALL.¹⁰

- Data from clinical trials show **TKIs are effective in improving outcomes for patients with Ph+ ALL, with long-term outcomes improving significantly since their introduction.**^{8,10}
- However, the development of BCR::ABL1 mutations can impact treatment response, making patients resistant to TKIs. Earlier incorporation of certain TKIs in treatment may help prevent the development of BCR::ABL1 mutations for patients with Ph+ ALL.^{11,12}

Apart from treatment with TKIs, stem cell transplantation (SCT) followed by maintenance therapy is a potentially curative option for patients with newly diagnosed Ph+ ALL.⁸ However, it may not be an appropriate treatment for all patients depending on their age and overall health status.¹³

- **For the third of patients with Ph+ ALL who are 60 years or older, treatment becomes more challenging with increasing age⁴, as 60-84% of older patients with ALL also have other existing medical conditions.¹³**

Unmet need

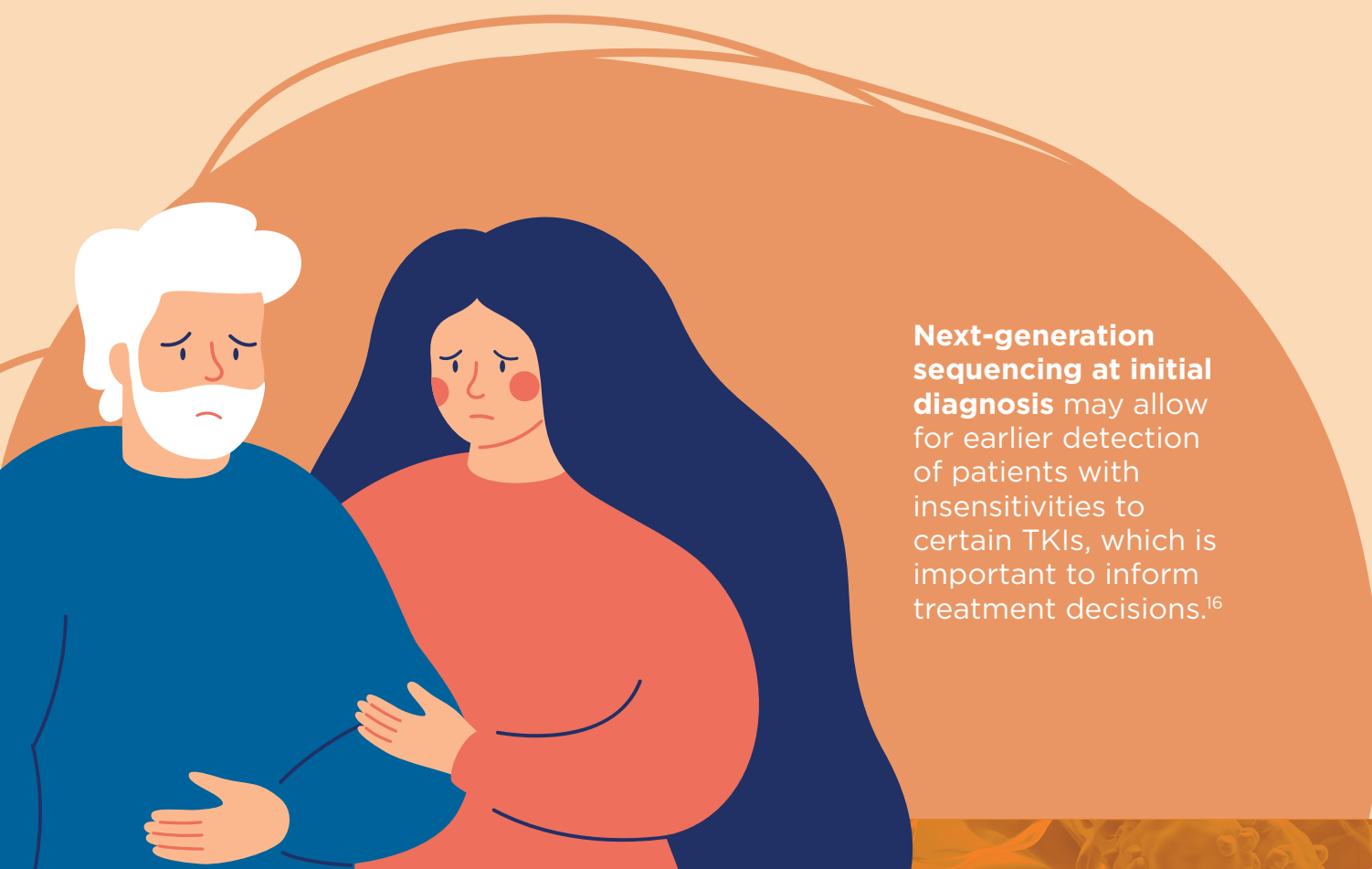
Relapse - when cancer returns after treatment - remains a significant challenge in treating Ph+ ALL, **occurring in 25% of patients who are first treated with TKIs.**¹⁴

- **75% of patients develop BCR::ABL1 mutations** after being treated with certain TKIs, which may cause patients to be resistant to later lines of therapy.⁸



- Outcomes for patients who relapse after initial treatment remains poor. **The response rate to treatment reduces from greater than 90% for newly-diagnosed patients to 30-40% for relapsed patients**, in addition to decreased survival rate.¹⁵
- This is why it is critical to ensure appropriate patients are being treated with suitable therapies available in the first line to help reduce the risk of relapse.¹⁴

Mutation screening is not a standardized test for all ALL patients before starting treatment with a TKI, despite the fact that BCR::ABL1 mutation may already exist for some patients prior to starting therapy.¹⁶



Next-generation sequencing at initial diagnosis may allow for earlier detection of patients with insensitivities to certain TKIs, which is important to inform treatment decisions.¹⁶

It is crucial to optimize care for people with newly diagnosed Ph+ ALL, which may enable them to achieve deep responses, prevent mutation development and sustain long-term survival outcomes.

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