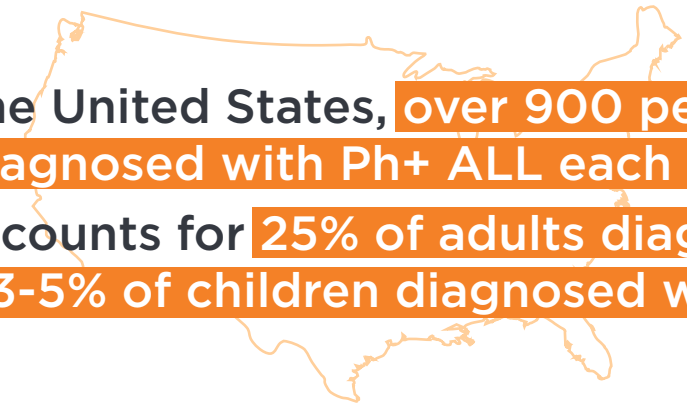
# ABOUT PHILADELPHIA CHROMOSOME-POSITIVE ACUTE LYMPHOBLASTIC LEUKEMIA (PH+ ALL)

Acute lymphoblastic leukemia (ALL) results from a mutation to a stem cell in the bone marrow. This injured 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.[3,5]**

**Ph+ ALL accounts for 25% of adults diagnosed with ALL and 3-5% of children diagnosed with ALL.[6,7]**

## Treatment Considerations for Ph+ ALL

Despite advancements in care, there are still significant challenges to address in the treatment of Ph+ ALL: [6,7]

Various tyrosine kinase inhibitors (TKIs), which are oral medications, in combination with chemotherapy, steroids or immunotherapies are often used to treat Ph+ ALL.[8]

- Currently, there are no TKIs approved in the U.S. for patients with newly-diagnosed Ph+ ALL.[9]
- Data from clinical trials have shown the potential for TKIs to improve outcomes for patients. **The long-term outcomes of patients with Ph+ ALL have improved significantly since the introduction of TKIs.**[6,8]
- However, 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.[10,11]

Stem cell transplantation (SCT) followed by maintenance therapy is a potentially curative option for patients with newly-diagnosed Ph+ ALL.[6] However, it may not be an appropriate treatment for all patients depending on their age and overall health status.[12]

- **For the third of patients with Ph+ ALL who are 60 years or older, treatment becomes more challenging with increasing age[4],** as 60-84% of older patients with ALL also have other existing medical conditions.[12]

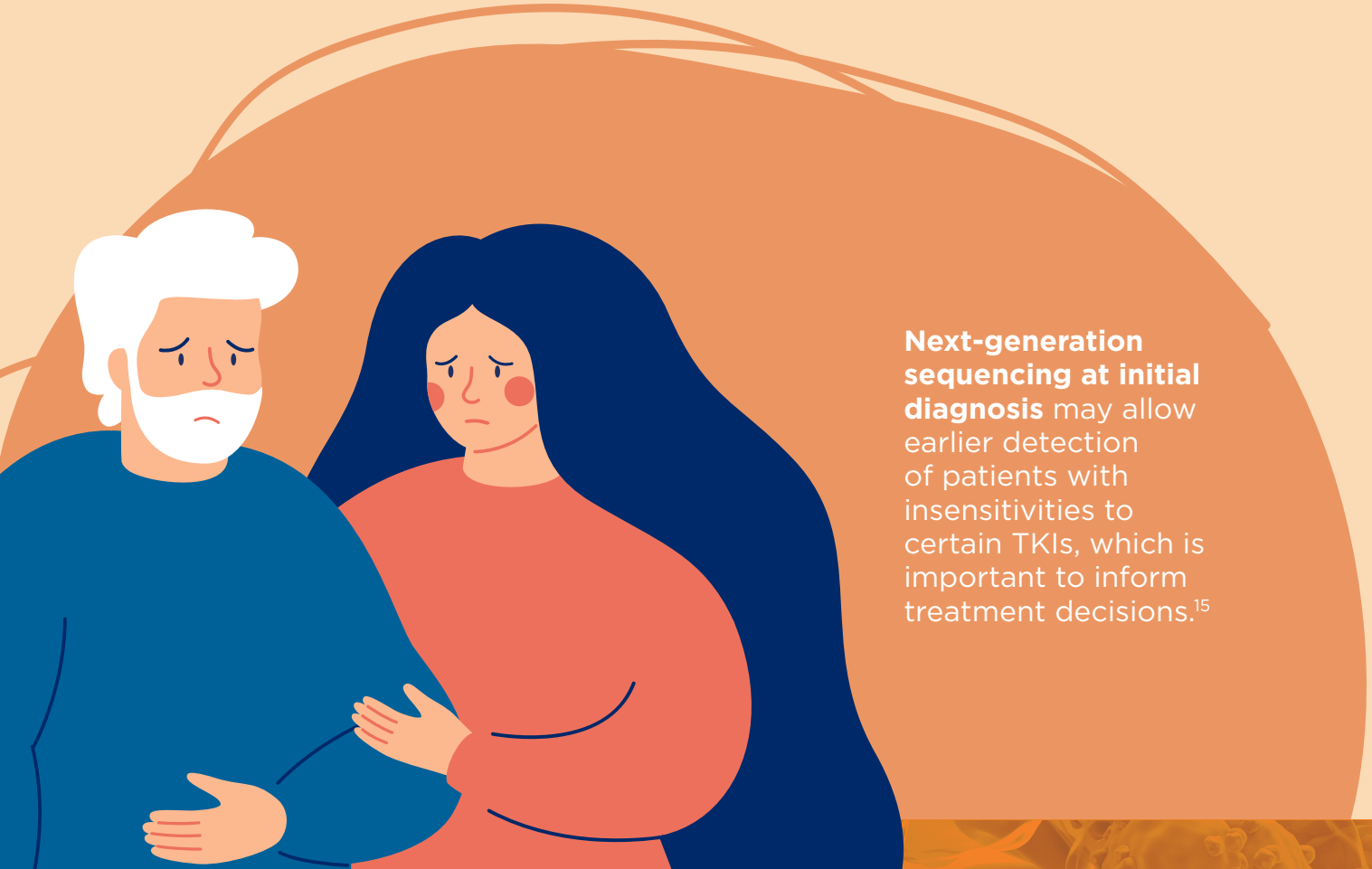
# Unmet need

## 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.[13]

- **75% of patients develop BCR::ABL1 mutations** after being treated with certain TKIs, which can cause treatment resistance.[6]

- 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.[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.[15]



**Next-generation sequencing at initial diagnosis** may allow earlier detection of patients with insensitivities to certain TKIs, which is important to inform treatment decisions.[15]

There is an urgent need to improve care for people with newly-diagnosed Ph+ ALL and enable patients to achieve deep and durable responses, prevent mutation development and sustain long-term survival outcomes.

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