

Good news for young patients with a leukemia subtype associated with a poor prognosis

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St. Jude Children's Research Hospital investigators found that adjusting treatment based on early response to chemotherapy made a life-saving difference to young patients with an acute lymphoblastic leukemia (ALL) subtype associated with a poor outcome. The study appeared in the September 20 edition of the *Journal of Clinical Oncology*.

The results are good news for children and adolescents with Philadelphia chromosome-like ALL (Ph-like ALL), a subtype that until now was associated with a poor prognosis. Ph-like ALL accounts for as much as 15 percent of the most common pediatric cancer. That cancer is called B-ALL because it affects white blood cells called B lymphocytes.

The study involved 344 children and adolescents with B-ALL, including 40 with the Ph-like ALL subtype. All were enrolled in a St. Jude clinical trial that used risk-directed [chemotherapy](#). The approach relied on a method pioneered at St. Jude to monitor and adjust treatment intensity based on the percentage of leukemic cells – or minimal residual disease (MRD) –in patient bone marrow at days 19 and 42 of chemotherapy.

Using MRD-based, risk-directed chemotherapy therapy, patients in this study had high rates of long-term and cancer-free survival regardless of their leukemia subtype. Overall, 92.5 percent of patients with Ph-like ALL in this study were alive five years after their cancer was discovered compared to 95.1 percent of other B-ALL patients.

"This study shows that by measuring [minimal residual disease](#) and using the results to guide treatment intensity, patients with Ph-like ALL can enjoy the same [high rates](#) of survival as other patients," said the study's corresponding author Ching Hon-Pui, M.D., chair of the St. Jude Department of Oncology.

When available, more sophisticated genetic testing should be used to identify which of the B-ALL patients with high levels of MRD have the Ph-like ALL subtype, Pui said. That is because many Ph-like ALL patients have genetic alterations that leave cancer cells vulnerable to available [cancer](#) drugs called ABL tyrosine kinase inhibitors (TKIs) and possibly other targeted therapies that are still experimental. Unlike conventional chemotherapy, TKIs kill more selectively and are less likely to damage healthy cells. Pui estimated that 20 percent of pediatric Ph-like ALL patients might be candidates for TKIs. "In the future, genetic testing will likely be used at diagnosis to identify Ph-like ALL and direct patients to the best targeted therapy, possibly including some drugs that are currently experimental," he said.

Ph-like ALL was first described in 2009 by two research groups, including investigators from St. Jude. The subtype is named for a chromosomal rearrangement known as the Philadelphia chromosome that is associated with a different ALL subtype. The Ph-positive and Ph-like ALL subtypes share similar patterns of gene expression. Patients with Ph-like ALL lack the fusion of the BCR and ABL1 genes that is a hallmark of Ph-positive ALL.

Previous studies of Ph-like ALL focused on high-risk patients whose treatment did not include risk-directed therapy based on MRD levels. This study included all eligible patients newly diagnosed with B-ALL who enrolled in the St Jude Total Therapy XV study between June 2000 and October 2007. Genomic testing was used to retrospectively diagnose Ph-like ALL.

MRD monitoring combined with conventional risk factors such as patient age and white blood count at diagnosis demonstrated that Ph-like ALL is not a uniformly high-risk disease. MRD also proved essential for identifying Ph-like ALL patients who can be cured with less-intensive chemotherapy. In this study, 40 percent of Ph-like ALL patients were classified with low-risk disease because they had other favorable clinical or biological features and no MRD at the end of remission induction, and received less-intensive treatment. Sixty percent of the 40 Ph-like ALL patients in this study were classified as having standard-risk or high-risk disease. The group included six [patients](#) who underwent bone marrow transplantation.

More information: jco.ascopubs.org/content/32/27/3012.long

Provided by St. Jude Children's Research Hospital

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