

# Improved diagnostic test benefits children with acute myeloid leukemia

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Early treatment response is a powerful predictor of long-term outcome for young patients with acute myeloid leukemia (AML). The information can help physicians decide whether a more intensive approach is needed. Research led by St. Jude Children's Research Hospital investigators has identified the best test for measuring that response and guiding therapy.

The method uses a laboratory technique called [flow cytometry](#), which makes it possible to identify a single cancer cell in 1,000 normal [cells](#) that remain in patient bone marrow after the initial intensive weeks of chemotherapy. St. Jude investigators were instrumental in developing the test for identifying very low levels of cancer called minimal residual disease.

An analysis published in the September 10 online edition of the [Journal of Clinical Oncology](#) showed that checking for minimal residual disease by flow cytometry was better than two other widely used methods for predicting patient survival. The results help identify who might benefit from more intensive therapy, including [bone marrow transplantation](#).

"These results will help establish flow cytometry testing for minimal residual disease as a routine tool for guiding therapy of [acute myeloid leukemia](#) and identifying patients early who are at risk of treatment failure," said Hiroto Inaba, M.D., Ph.D., an associate member of the Department of Oncology at St. Jude. He is the study's first and corresponding author.

Flow cytometry uses a laser to help distinguish cancer cells from normal cells based on different cell surface markers and other molecules. Dario Campana, M.D., Ph.D., led the successful St. Jude effort to develop the test about 15 years ago. Campana, now at the National University of Singapore, is the paper's senior author.

Such testing is widely used to guide treatment of the most common [childhood cancer](#), [acute lymphoblastic leukemia](#) (ALL). AML targets different [white blood cells](#) than ALL does. AML also affects fewer children and adolescents, about 500 annually in the U.S., and has a lower survival rate. Although 94 percent of St. Jude ALL patients can now look forward to becoming long-term survivors, the figure is 71 percent for young AML patients.

AML treatment response is evaluated on day 22 of therapy as well as at the end of each treatment phase and serves as a powerful predictor of patient survival. The results are used to guide ongoing therapy and identify patients who are candidates for more intense treatment.

For decades, physicians have relied on the microscope to evaluate patient response to therapy. Patients are considered to be in remission if a bone marrow examination finds [cancer cells](#) account for fewer than five in 100 cells. Flow cytometry and another [laboratory technique](#) called polymerase chain reaction (PCR) were also developed to help gauge treatment response. PCR is used to monitor genes created when chromosomes break and swap pieces. The genes are found in about half of all pediatric AML cases.

This study is the most comprehensive effort yet comparing the power of the three approaches to predict the AML treatment outcome. The work involved 203 AML patients enrolled in a clinical trial called AML02. St. Jude led the multi-institution study of young AML patients whose disease was diagnosed between 2002 and 2008. The project marked the

first time minimal residual disease was used to guide therapy. During the study researchers examined 1,514 patient bone marrow samples by flow cytometry. Of those samples, 1,382 also had information regarding microscopic evaluation and 508 of PCR testing.

The analysis showed that minimal [residual disease](#) measured by flow cytometry was an independent predictor of patient outcome. Finding even one leukemia cell in 1,000 normal cells in bone marrow after the first or second round of therapy was associated with a worse prognosis and a greater risk of relapse or [treatment failure](#).

Researchers concluded microscopic examination had limited value for gauging treatment response. Problems ranged from an inability to distinguish between cells destined to become leukemia cells and normal blood cells to classifying about 10 percent of patients as being in remission when flow cytometry identified leukemia cells in the same bone marrow.

Investigators also concluded that flow cytometry rendered PCR testing unnecessary for most AML patients. The analysis found PCR testing generally overestimated the presence of leukemia cells. In this study, PCR identified 197 of 311 patient samples as containing leukemia cells. Flow cytometry of the same samples showed just 19 actually harbored detectible [minimal residual disease](#). Researchers did find PCR testing valuable in predicting outcome and guiding therapy for a subgroup of AML patients with mixed lineage leukemia (MLL) gene changes.

Provided by St. Jude Children's Research Hospital

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