

Chemotherapy proves life-saving for some leukemia patients who fail induction therapy

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An international study found that bone marrow transplants are not the best option for some young patients with acute lymphoblastic leukemia (ALL) who fail to attain clinical remission after the initial weeks of intense chemotherapy known as induction therapy.

The largest study ever of such pediatric ALL [patients](#) identified a subset of young children who achieved 10-year survival rates of 72 percent after additional chemotherapy rather than bone marrow transplantation. The patients are among the estimated 85 percent of children with ALL whose cancer begins in [white blood cells](#) destined to become [B cells](#).

The results appear in the April 12 edition of the [New England Journal of Medicine](#). The study involved researchers from 14 research groups in the U.S., Europe and Asia.

"Induction failure is a rare event, affecting just 2 to 3 percent of all pediatric ALL patients. But these children are at very high risk for a bad outcome and were always considered candidates for [bone marrow transplantation](#)," said Ching-Hon Pui, M.D., chair of the St. Jude Children's Research Hospital Department of Oncology. "These results tell us that induction failure should no longer be considered an automatic indication for a transplant." Pui is the study's corresponding author.

Improvements in both chemotherapy and transplantation prompted investigators to revisit the question of optimal care for these patients. But no single institution or nation had enough patients to answer it. "This

study shows the importance of [international collaboration](#) to advance the treatment outcome for these patients," said first author Martin Schrappe, M.D., University Medical Center Schleswig-Holstein, Kiel, Germany.

Investigators evaluated the outcomes of 44,017 ALL patients age 17 and younger whose cancer was discovered during a 15-year period ending in December 2000. Each was treated on a clinical trial at one of the centers participating in this international collaborative analysis. St. Jude patients were part of the study. Researchers tracked 1,041 patients whose cancer did not go into remission following four to six weeks of induction therapy.

Historically, the prognosis has been grim for patients who fail induction therapy. While overall long-term survival for childhood ALL patients climbed to 80 percent during the 15 years covered in this study, it was just 32 percent for patients who did not enter remission after the first intense weeks of treatment. The definition of induction failure differed slightly among the clinical trials included in this analysis.

The study found long-term [survival rates](#) of 72 percent among some young patients with B-lineage ALL treated with additional chemotherapy following induction therapy failure. The patients were ages 1 through 5 when their cancer was found and many had more than 50 chromosomes in their leukemia cells, rather than the normal number of 46 chromosomes. Together they accounted for about 25 percent of patients whose disease did not go into remission following induction therapy.

The children who benefited from additional chemotherapy also had no other markers of high risk, including high white blood cell counts or chromosomal rearrangements involving the MLL gene.

The study found transplants remain the best hope for many other young ALL patients who fail induction therapy. The patients included those

whose cancer originated in white blood cells known as T cells. T cell ALL accounts for 12 to 15 percent of childhood ALL, but about 38 percent of patients in this study. The transplants involve killing the patient's own diseased bone marrow and replacing it with blood-producing stem cells from a genetically matched donor. The procedure leaves patients at risk for a variety of immediate and chronic health problems.

Patients with a chromosomal rearrangement known as the Philadelphia chromosome were not included in the analysis because new drugs have led to a dramatic improvement in their outcome. About 13 percent of ALL induction treatment failures involved patients with the genetic alteration.

Provided by St. Jude Children's Research Hospital

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