[News * Analysis * Commentary * Controversy]

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Exercise: Finding the Right Rx for Cancer Patients

BY SARAH DIGIULIO

The question is no longer whether or not exercise is safe for cancer patients. Evidence shows it is not only not harmful, but can also relieve fatigue, protect bones, enhance cardiopulmonary functions, and help psychologically. Here's our roundup of recent findings, including a new study of the benefits of community-based, individually tailored group exercise programs for cancer survivors.

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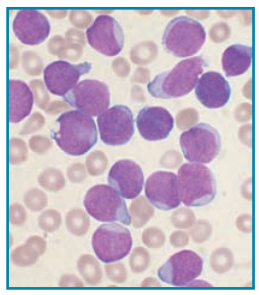
ALLEN LICHTER: ASCO's Top 5 Questionable Procedures p.5

Highlights from AACR Annual Meeting pp.13, 20, 26

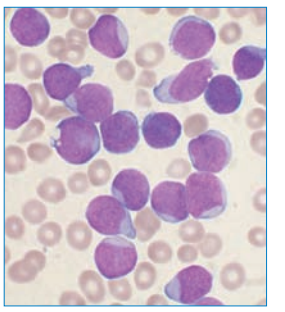


Pediatric ALL: Chemo May Save Some Children Not Helped with Induction p.17

***OT* iPad App!**

PERIODICALS

Chemotherapy May Save Some Children with ALL Not Helped with Induction Therapy



BY SARAH DIGIULIO

For a subset of pediatric acute lymphoblastic leukemia (ALL) patients who do not have a clinical remission after induction therapy (typically intense chemotherapy), additional chemotherapy may be more effective than transplantation, which has been the standard second step, according to the results of a large, international, retrospective study.

The study, published in the *New England Journal of Medicine* (***2012;366:1371-1381***), reviewed 44,017 cases of pediatric ALL from 14 cancer care centers in the U.S., Europe, and Asia, making it the largest study ever of these pediatric ALL patients.

"We thought patients who fail chemotherapy would probably be refractory to all chemotherapy, and that you would therefore need to do transplantation, but that turned out to not be true for some types of leukemia," said the corresponding author, Ching-Hon Pui, MD, Chair of the St. Jude Children's Research Hospital Department of Oncology, in a telephone interview. Subsequent consolidation therapy with high-dose chemotherapy can save many children with precursor B-cell leukemia without other adverse features, he and his colleagues found.

Of the children with ALL in the study (first author was Martin Schrappe, MD), 1,041 had failed to respond to induction therapy and 32 percent of those patients survived for at least 10 years. But, the survival rate jumped to 72 percent for the subset of children with B-cell ALL who had

> 32 percent of the children reached 10-year survival—but the survival rate was 72 percent for the subset of patients with B-cell ALL treated with a second round of chemotherapy only.

received a second round of chemotherapy only. This subset represented about 25 percent of the patients for whom the initial chemotherapy had failed.

"These results tell us that induction failure should no longer be considered an automatic indication for a transplant," Pui said.

Transplant is typically the next step after induction failure because it is the most aggressive treatment and includes a mild chemotherapy dose, Pui explained. But, two drugs not used during induction—methotrexate and mercaptopurine—are particularly effective for B-cell ALL patients, and are most effective for

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→CHEMO ALL

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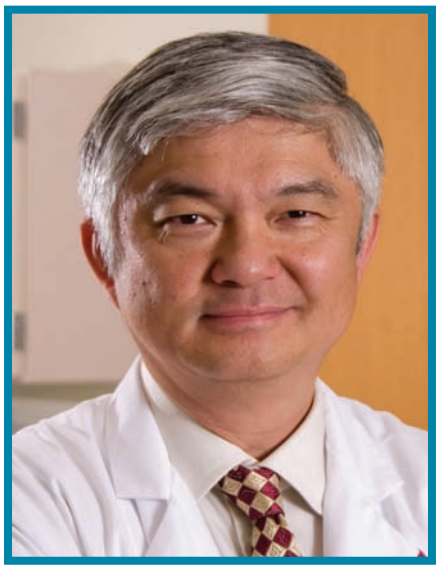


CHING-HON PUI, MD: "We thought patients who fail chemotherapy would probably be refractory to all chemotherapy, and that you would therefore need to do transplantation. But that turned out to not be true for some types of leukemia."

those between age 1 and 6, and those with high hyperdiploidy, the study found.

While that subset of children did not seem to benefit from allogeneic transplantation, the researchers did conclude that transplant therapy was still most effective for the subset of patients with T-cell ALL, and was more effective than further chemotherapy alone.

"This is an important implication," said Pui, who will receive ASCO's Pediatric Oncology Award at this year's Annual Meeting. "When a doctor fails a patient with induction therapy, they need to know other features before they determine whether they should recommend transplantation."

Key Implications

Asked for his opinion of the study for this article, Peter Adamson, MD, Director or Experimental Therapeutics in Oncology at Children's Hospital of Philadelphia, pointed out that one of the most important takeaways from this research is realizing that the most effective means of curing ALL patients is likely personalizing therapies to various subsets of patients—however small those populations are. Induction failure occurs in just two to three percent of children with ALL, and the subset of patients with precursor B-cell ALL accounts for only about 25 percent of those patients.

"I think the main lesson is that in making future advances in curing ALL—because the subsets of populations that we need to study are getting smaller, including the subsets where induction therapy fails—we will need to collaborate, and collaborate on a large scale. And, secondly, we learned that some of our assumptions so far turned out to be incorrect," Adamson said in a phone interview. He is also Chief of the Division of Clinical Pharmacology and Therapeutics at the hospital and Professor of Pediatrics at the Perelman School of Medicine at the University of Pennsylvania.

> Even though the percentage of children with ALL who do not respond to induction therapy is very small, it is one of the most likely predictors of overall failure and is indicative of the highest risk of a negative disease outcome.

PETER ADAMSON, MD: "Some of our assumptions so far of which patients relapse are going to turn out not to be correct."

'Practice Changing'

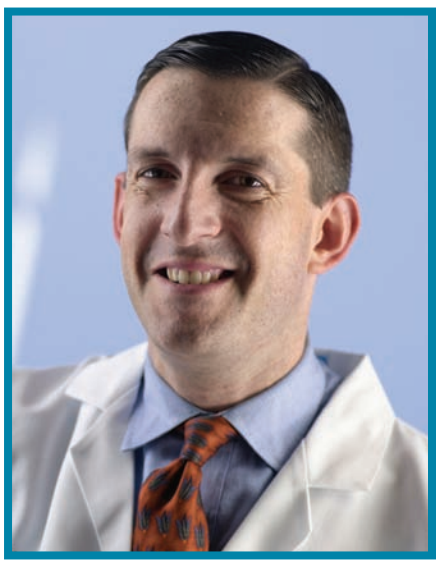
And *OT*'s Clinical Advisory Editor for Hematology/Oncology, Mikkael Sekeres, MD, MS, Director of the Leukemia Program and Chair of the Hematology/Oncology Pharmacy & Therapeutics Committee at the Cleveland Clinic Taussig Cancer Institute, predicted that for this small subset of patients, the evidence from this study may change the paradigm of treatment

"Those with precursor B-cell ALL without other adverse features may actually have at least as good if not a better outcome with subsequent chemotherapy, as compared with hematopoietic stem cell transplantation, which in itself may redefine whether or not these patients were truly induction 'failures,' or whether our traditional assessment of failure in pediatric ALL may be premature," he said.

Adamson noted that future research needs to look at individual subsets of patients and what makes them unique. "We need to understand the heterogeneity—what are the features in the leukemia in these children that are going to predispose them to this outcome," he said.

> "Induction failure should no longer be considered an automatic indication for a transplant."

Sekeres said that future research is also needed to see if the findings are consistent for different age groups. "Whether these results can be translated to the treatments of adults with ALL remains to be seen," he said.



MIKKAEL SEKERES, MD, MS: "The findings may redefine whether or not these patients were truly induction 'failures,' or whether our traditional assessment of failure in pediatric ALL may be premature."

Researchers Dedicated the Study to James Nachman

The researchers dedicated the study to James B. Nachman, MD, who died last year of a suspected heart attack while on a rafting trip in the Grand Canyon.

"He contributed, with a truly global view and outstanding personal dedication, to this and many other important scientific papers in the field of pediatric leukemia," the authors wrote.