



Total XV protocol significantly improves survival in older adolescents with leukemia

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Motivated by the fact that older children who participate in acute lymphoblastic leukemia (ALL) trials relapse more often and fare worse overall than do younger children, researchers at St. Jude Children's Research Hospital in Memphis, Tennessee, used a new treatment protocol to achieve cure rates of 88% for the older adolescents. The study, which was recently published in the *Journal of Clinical Oncology*, involved 45 older adolescents and 453 younger patients. The paper also included details of 44 older and 403 younger patients treated in earlier studies.¹

Researchers compared the long-term survival rates of patients in two age groups who were treated according to one of two St. Jude protocols. Thus patients treated between 2000 and 2007 were compared with those enrolled in earlier St. Jude protocols between 1991 and 1999.

RISING SUCCESS RATES

Approximately 59% of older adolescents who were treated between 1991 and 1999 were considered cured, while the cure rate was more than 88% for children aged 1 to 14 years who were treated during the same time period. With the new protocol, however, outcomes were much better. Between 2000 and 2007, the overall survival rates for older adolescents reached almost 88%,

and the long-term survival rates for younger children with acute lymphoblastic leukemia who were treated at St. Jude reached almost 94%. This is in contrast to the national 5-year survival rate of approximately 61% for ALL patients aged 15 to 19 years who were treated between 2000 and 2004.

"The most important finding from our study is that almost 90% of older adolescents with ALL can be cured today, and the vast majority of them do

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not need bone marrow transplantation," said Ching-Hon Pui, MD, chair of the Department of Oncology at St. Jude and lead author of the study. "There is always the perception that adolescents between the ages of 15 and 18 with this disease have very poor outcomes. I think this study should change the perception that this is a poor risk group of patients."¹

FEWER LATE TREATMENT EFFECTS

In addition to having much better survival rates, patients treated with the new

protocol were less likely to have late treatment effects, such as second cancers and infertility. Researchers explained that the reason for this is the reduction in use or elimination of medications that cause those side effects. "Not only have we increased the cure rate, but we have also improved the long-term quality of life for our patients," Dr. Pui said.

TOTAL XV PROTOCOL

The new treatment protocol, known as Total XV, was innovative in several ways:

- Instead of administering radiation to the brain, patients were given chemotherapy to prevent relapse of the CNS and to reduce their risk of developing future neurocognitive complications. As a result, none of the older patients experienced CNS relapses.
- The protocol utilized targeted IV high-dose methotrexate and asparaginase for the older patients.
- The team monitored patient compliance closely. They utilized blood tests to identify patients with very low or undetectable levels of mercaptopurine, an indication that patients were not taking their medication as directed. Mercaptopurine levels went up after the staff reminded patients and their families how important it was to follow the protocol strictly.
- Researchers concluded that adolescents and young adults with acute

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lymphoblastic leukemia do better when treated on pediatric regimens rather than adult protocols.

- This was the first time that a patient's initial treatment response has been used to guide ongoing care. The technique involves measuring cancer cells that survived initial therapy, also known as the minimal residual disease (MRD). According to Dr. Pui, "MRD screening allowed us to catch patients who would previously not have been identified as poor responders to therapy and to treat them more intensively."

PEDIATRIC PROTOCOLS BETTER FOR ADOLESCENTS

In the past, adolescents older than 14 years who developed ALL were not as likely to survive as were younger patients, for a

number of reasons: Adolescents are more prone to high-risk subtypes of the disease, their cancer cells can be more resistant to current anticancer medication, and the treatment tends to be more toxic.

"The challenge is to get adolescents on the right amount of drug while avoiding toxicity," said Mary Relling, PharmD, chair of the Pharmaceutical Sciences Department at St. Jude and coauthor of the research paper. "In Total XV, we seem to have struck the right balance. There are a lot of data to show that young adults with ALL [who are] treated on pediatric protocols have fewer relapses than similar patients treated on adult leukemia protocols," said Dr. Relling. She added that the results suggest that patients in their 20s and 30s who have acute lymphoblastic leukemia might benefit from the addition of high-dose

methotrexate and asparaginase in their treatment. Although both drugs block proliferation of cancer cells, they are not often used in treating adults, partially because they lead to more complications as patients get older.

Dr. Relling said, "The next steps for our research are to figure out how to maintain these very high cure rates and to try to decrease at least some of the toxicity and side effects, especially in the older children." ■

Bette Kaplan is a medical writer based in Tenafly, New Jersey.

REFERENCE

1. Pui CH, Pei D, Campana D, et al. Improved prognosis for older adolescents with acute lymphoblastic leukemia. *J Clin Oncol*. 2011;29(4):386-391.