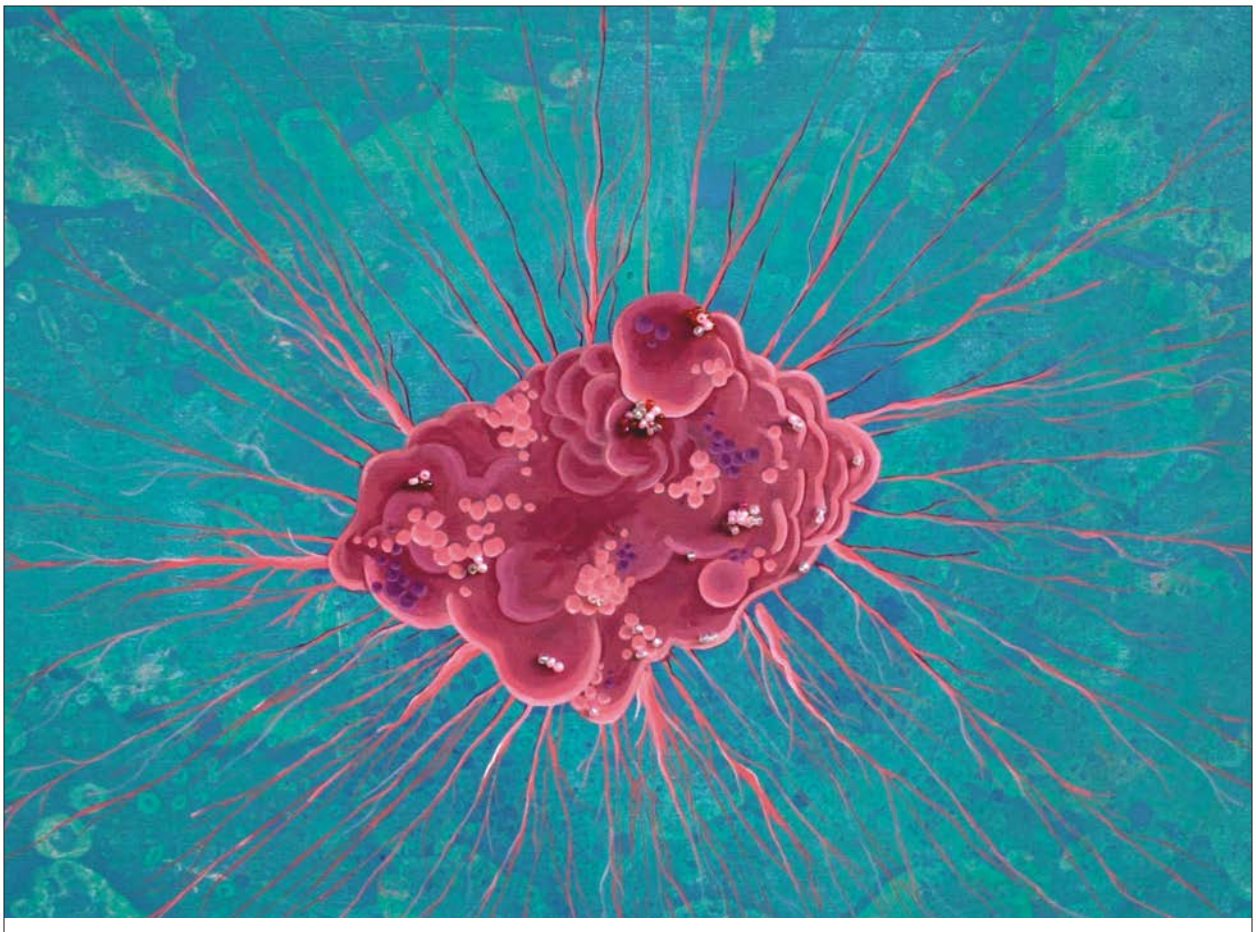

International Journal of Cancer Research

ISSN 1811-9727

Academic Journals Inc.

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Intensive Chemotherapy Can Dramatically Boost Survival of Older Teenage Leukemia Patients

More effective risk-adjusted chemotherapy and sophisticated patient monitoring helped push cure rates to nearly 88 percent for older adolescents enrolled in a St. Jude Children's Research Hospital acute lymphoblastic leukemia (ALL) treatment protocol and closed the survival gap between older and younger patients battling the most common childhood cancer.

A report online in the December 20 edition of the Journal of Clinical Oncology noted that overall survival jumped 30 percent in the most recent treatment era for ALL patients who were age 15 through 18 when their cancer was found.

The study compared long-term survival of patients treated between 2000 and 2007 in a protocol designed by St. Jude investigators with those enrolled in earlier St. Jude protocols. About 59 percent of older patients treated between 1991 and 1999 were cured, compared with more than 88 percent of children ages 1 through 14 treated during the same period. But overall survival for older patients rose to almost 88 percent between 2000 and 2007, when long-term survival of younger patients soared to about 94 percent. Nationally, about 61 percent of ALL patients age 15 to 19 treated between 2000 and 2004 were still alive five years later.

Not only did more patients in the recent treatment era survive, but Ching-Hon Pui, M.D., Chair of the St. Jude Department of Oncology and the paper's Lead Author, said they are also less likely to suffer serious late treatment effects, including second cancers and infertility. That is because the regimen, known as Total XV, eliminated or dramatically reduced reliance on drugs associated with those side effects.

The protocol also replaced radiation of the brain with chemotherapy as a strategy for preventing relapse in the central nervous system and for reducing the risk of later neuro-cognitive problems. None of the adolescents suffered central nervous system relapses. "Not only have we increased the cure rate, but we have also improved the long-term quality of life for our patients," Pui said.

Historically, individuals who develop ALL after age 14 were less likely to survive their disease than were younger patients. Older teenagers are more likely to have high-risk subtypes of the disease, their cancer cells are more likely to be resistant to current anti-cancer drugs and they tend to have more toxicity from therapy. "The challenge is to get adolescents on the right amount of drug while avoiding toxicity. In Total XV we seem to have struck the right balance," said Mary Relling, Pharm.D., chair of St. Jude Pharmaceutical Sciences Department and co-author of the research.

The findings come amid growing evidence that adolescents and young adults with ALL do better when treated on pediatric rather than adult protocols. "There are a lot of data to show that young adults with ALL treated on pediatric protocols have fewer relapses than similar patients treated on adult leukemia protocols," Relling said. She noted that these results suggest ALL patients in their 20s and 30s might benefit from adding high-dose methotrexate and asparaginase to treatment. Both drugs block proliferation of cancer cells. They are not widely used in adult cancer treatment, in part because increased age is associated with more complications. Pui said Total XV also demonstrated the vast majority of older adolescents can be cured without undergoing a bone marrow transplant. "This lesson should be extended to young adults," he added.

Total XV incorporated several treatment innovations, including greater use of targeted intravenous high-dose methotrexate and asparaginase for older patients. The

study included 45 older adolescents and 453 younger patients. 44 older and 403 younger patients treated in the earlier studies were also included in this report.

Pui said patient compliance was also closely monitored. Blood tests helped identify patients with very low or no detectable amount of the drug mercaptopurine, a sign the drug was not being taken as directed. Pui said levels of the chemotherapy agent rose after patients and families were reminded of the importance of strict treatment adherence.

For the first time, a patient's initial response to treatment was used to guide ongoing care. The technique was pioneered at St. Jude and involves measuring cancer cells or the Minimal Residual Disease (MRD) that survived initial therapy. "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," Pui said.

The other authors are Dequing Pei, Dario Campana, John Sandlund, Sue Kaste, Raul Ribeiro, Jeffrey Rubnitz, Elaine Coustan-Smith, Sima Jeha, Cheng Cheng, Monika Metzger, Deepa Bhojwani, Hiroto Inaba, Susana Raimondi, Mihaela Onciu, Scott Howard, Wing Leung, James Downing and William Evans, all of St. Jude; and W. Paul Bowman of Cook Children's Hospital, Fort Worth.

The research was supported in part by the National Institutes of Health, the American Cancer Society and ALSAC.

Ching-Hon Pui, Deqing Pei, Dario Campana, W. Paul Bowman, John T. Sandlund, Sue C. Kaste, Raul C. Ribeiro, Jeffrey E. Rubnitz, Elaine Coustan-Smith, Sima Jeha, Cheng Cheng, Monika L. Metzger, Deepa Bhojwani, Hiroto Inaba, Susana C. Raimondi, Mihaela Onciu, Scott C. Howard, Wing Leung, James R. Downing, William E. Evans, and Mary V. Relling. Improved Prognosis for Older Adolescents With Acute Lymphoblastic Leukemia. Journal of Clinical Oncology, December 20, 2010 DOI: 10.1200/JCO.2010.32.0325