New regimens improve survival for children and young adults with T-cell cancers

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In a federally funded, randomized phase III clinical trial performed by the Children's Oncology Group (COG), 90 percent of children and young adults with T-cell acute lymphoblastic leukemia (T-ALL) or T-cell lymphoblastic lymphoma (T-LL) were alive four years after starting treatment regimens on this trial, and 84 percent were cancer free. These are the highest survival rates for these T-cell malignancies reported to date, according to the authors.

The addition of nelarabine (Arranon) to standard chemotherapy provided further benefit for the group of patients with moderate or high risk of T-ALL recurrence—at four years 89 percent of those who received nelarabine were leukemia-free vs. 83 percent of those who did not. The study will be presented at the upcoming 2018 ASCO Annual Meetingin Chicago.

"T-cell ALL is a disease that requires the use of a very intense and complex chemotherapy regimen. Historically, about 80 percent of people live at least four years after being treated for their disease, but we felt we could and must do better," said lead study author Kimberly Dunsmore, MD, professor, Virginia Tech Carilion School of Medicine in Roanoke. "Our trial shows that we could further increase survival rates by about 10 percent, which is very encouraging."

About the Study

The trial, begun in 2007, enrolled patients 1-30 years of age with either T-ALL (94 percent of trial participants) or T-LL (6 percent of participants). With 1,895 patients, this is the largest randomized clinical trial ever performed in these diseases.

The trial had four arms, with all patients receiving the standard, complex, multi-drug chemotherapy regimen known as COG augmented Berlin-Frankfurt-Munster (aBFM) chemotherapy.1In addition to receiving aBFM, patients were randomly assigned to also receive either high-dose methotrexate (a chemotherapy) in a hospital or escalating dose methotrexate (a regimen that starts with low doses of methotrexate, gradually increased over time) in an outpatient setting.

The group of patients with moderate or high risk of cancer recurrence were also randomly assigned to receive or not receive nelarabine, in addition to chemotherapy, and cranial radiation (to prevent or treat brain metastases).

Nelarabine was approved in 2005 by the FDA for the treatment of people with T-ALL and T-LL that had progressed after at least two chemotherapy regimens. Unlike the trials that led to the FDA approval, nelarabine was tested in newly diagnosed patients in this trial.

Key Findings

- Overall, 90.2 percent of patients treated in this trial lived at least four years, and 84.3 percent had no sign of cancer at four years.
- In the group of patients with T-ALL who had increased risk of recurrence, 88.9 percent of those who received nelarabine were leukemia-free at four years compared to 83.3 percent of those not treated with nelarabine.
- While patients with T-LL did not benefit from the addition of nelarabine, more than 85 percent lived for four years without

signs of disease.

- Contrary to results from previous, smaller trials, patients with T-ALL who received escalating doses of methotrexate did better than those who received high-dose methotrexate (four-year disease-free survival with escalating dose was 89.8 percent vs. 78 percent with high-dose).
- Among T-ALL patients randomly assigned to receive both nelarabine and escalating doses of methotrexate, 92.2 percent were leukemia-free at four years.
- Patients who did not have cancer remission following the initial (induction) phase of chemotherapy were assigned to receive high-dose methotrexate and nelarabine; 54.8 percent of survived four years without signs of the disease. This is a significant improvement, as historically only about 20 percent of people with T-ALL who did not experience cancer remission lived another three years, according to the authors.

Most doctors are moving to decreasing the use of cranial radiation for T-cell leukemia as late side effects can occur after cranial radiation. Late side effects include changes in cognitive abilities, learning disabilities, neuroendocrine changes, and development of secondary malignancy. The next step will be for clinicians to examine the implications and benefits that may accrue when using nelarabine in chemotherapy protocols without cranial radiation.

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