ネララビンはT細胞性悪性腫瘍の生存率を改善する (Abstract 10500)

新たな治療法は小児および若年成人T細胞性悪性腫瘍の生存率を改善する

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

T細胞性急性リンパ芽球性白血病(T-ALL)またはT細胞性リンパ芽球性リンパ腫(T-LL)を有する小児および若年成人の90%が標準的な化学療法にネララビンを上乗せすることで4年間生存し84%が再発しなかった、との第III相臨床試験の結果が2018 ASCO Annual Meetingで発表された。この結果は、これらのT細胞性悪性腫瘍に対してこれまで報告された生存率の中で最も高いものである。標準的な化学療法にネララビンを上乗せすることで、T-ALLの中等度または高リスク患者群に対してさらなるベネフィットが得られた; 4年後、ネララビン投与群の89%に再発がなかったのに対し、非投与群におけるその割合は83%であった。

Full Text

In a randomized phase III clinical trial performed by the Children's Oncology Group (COG), 90% 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% 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 to standard chemotherapy provided further benefit for the group of patients with moderate or high risk of T-ALL recurrence – at four years 89% of those who received nelarabine were leukemia-free vs. 83% of those who did not. The study is presented at the 2018 ASCO Annual Meeting in Chicago.

"T-cell ALL is a disease that requires the use of a very intense and complex chemotherapy regimen. Historically, about 80% 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, Virginia, USA. "Our trial shows that we could further increase survival rates by about 10%, which is very encouraging."

The trial, begun in 2007, enrolled patients 1-30 years of age with either T-ALL (94% of trial participants) or T-LL (6% 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. In addition to receiving aBFM, patients were randomly assigned to also receive either high-dose methotrexate in a hospital or escalating dose methotrexate 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.

Key findings:

- Overall, 90.2% of patients treated in this trial lived at least four years, and 84.3% had no sign of cancer at four years.
- In the group of patients with T-ALL who had increased risk of recurrence, 88.9% of those who received nelarabine were leukemia-free at four years compared to 83.3% of those not treated with nelarabine.
- While patients with T-LL did not benefit from the addition of nelarabine, more than 85% 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% vs. 78% with high-dose).
- Among T-ALL patients randomly assigned to receive both nelarabine and escalating doses of methotrexate, 92.2% were leukemia-free at four years.
- Patients who did not have cancer remission following the induction phase of chemotherapy were assigned to receive high-dose methotrexate and nelarabine; 54.8% of survived four years without signs of the disease. This is a significant improvement, as historically only about 20% 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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