Clofarabine and cytarabine for acute myeloid leukaemia

Children with acute myeloid leukaemia could be treated with a less toxic regimen of clofarabine and cytarabine, avoiding exposure to anthracyclines and etoposide, according to new research.

In the randomised, phase 3, AML08 trial, Jeffrey E Rubnitz (St Jude Children's Research Hospital, Memphis, TN, USA) and colleagues randomly assigned (1:1) 262 paediatric patients (aged <22 years) with untreated acute myeloid leukaemia to receive either clofarabine 52 mg/m^2 and cytarabine 1g/m^2 on days 1–5 (n=129) or high-dose cytarabine 3 g/m^2 every 12 h on days 1, 3, and 5, daunorubicin 50 mg/m^2 on days 2, 4, and 6, and etoposide 100 mg/m^2 on days 2–6 (n=133) during the first induction. Patients received a second induction of low-dose cytarabine, daunorubicin, and etoposide alone or in combination with sorafenib or vorinostat, followed by two or three courses of consolidation (chemotherapy or hematopoietic stem cell transplantation). The primary endpoint was minimal residual disease (MRD) negativity at day 22.

MRD at day 22 was present in 57 (47%) of 121 evaluable patients in the clofarabine plus cytarabine group and in 42 (35%) of 121 patients in the high-dose cytarabine, daunorubicin, and etoposide group (odds ratio 1·86 [95% CI 1·03–3·41], p=0·04). However, the proportion of patients with complete remission did not differ between the groups (93·0% [95% CI 87·2–96·8] with clofarabine and cytarabine *vs* 92·5% [86·6–96·3] with high-dose cytarabine, daunorubicin, and etoposide). 3-year event-free survival (p=0·94) or overall survival (p=0·10) did not differ between groups.

Rubnitz said "The use of clofarabine during induction therapy allowed us to reduce daunorubicin exposure by 150 mg/m^2 without compromising survival. However, the use of natural killer cell therapy did not reduce the risk of relapse. We are now exploring new agents that were not available when the AML08 trial commenced."

Elihu Estey (Fred Hutchinson Cancer Research Center, Seattle, WA, USA) said "it may be possible to replace anthracyclines with clofarabine during induction therapy in children, which should reduce the eventual likelihood of long-term anthracycline-induced clinical heart disease." He added that "this study does not prove that clofarabine plus high-dose cytarabine is superior to the current standard. Rather the study shows that in conjunction with certain post-course 1 therapy the clofarabine combination may be superior, at least in reducing the deleterious effect of MRD."

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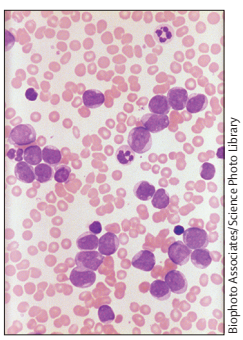

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For the **study by Rubnitz and colleagues** see *J Clin Oncol* 2019; published online June 27. DOI:10.1200/JCO.19.00327