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50 Years Ago in *The Journal of Pediatrics*

Searching for Survivors–Chemotherapy for Treatment of Acute Myelogenous Leukemia

Freedman MH, Finklestein JZ, Hammond GD, Karon M. The effect of chemotherapy on acute myelogenous leukemia. J Pediatr 1971;78:526-32

Until the late-1950s, acute myelogenous leukemia (AML) in children was a death sentence. Most were offered supportive care and survived only a few months. This seminal publication by Freedmen et al reported a high morphologic remission rate of 70% and prolonged median survival of 9.5 months in 60 patients with AML treated from 1956 to 1968 with combination chemotherapy. This study was the start of 50 years of effective combination chemotherapy regimens used for AML.

Since then, we have optimized the chemotherapy backbone to include high-dose cytarabine and anthracyclines. We can now better stratify patients at high risk of relapse by measuring minimal residual disease by flow cytometry and identify chemoresistance-conferring mutations with next-generation sequencing.[1] Stem cell transplant, which was just being investigated at the time of Freedman et al's study, has since been found to be curative even in the end stages of AML by the 1970s[2] and is currently the treatment of choice for high-risk AML. Second-generation molecular inhibitors of fms-related receptor tyrosine kinase 3 internal tandem duplications and activating tyrosine kinase domain mutations, DNA methyltransferase, and isocitrate dehydrogenase, B-cell lymphoma 2, along with antibody-drug conjugates and bispecific targeted antibodies such as gemtuzumab ozogamicin and flotetuzumab have been developed and are beginning to change the treatment paradigm in AML. Based on 50 years of treatment advances in AML, the 5-year event-free survival rates for childhood AML are now 60%-70%, with survivors living late into adulthood. Despite these advances, high-risk AML is still associated with poor outcomes and presents a major challenge to oncologists. With the advances in CAR (chimeric antigen receptor)-T technology, immunology, pharmacogenomic research, and novel targeted agents, just imagine how pediatric AML therapy will change in the next 50 years!

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