What are the treatment options for children with newly diagnosed treatment-related AML?

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Good afternoon everybody. Welcome to *Managing AML*. My name is Andy Kolb, I am a pediatric oncologist. I'm frequently asked, “What are the treatment options for children with newly diagnosed treatment-related AML?” This is certainly a challenge and it depends a lot on the comorbidities that a patient brings to that diagnosis. Patients who are many years out from treatment for their primary malignancy may be able to tolerate more therapy than children who are closer to the diagnosis of their primary therapy. Sometimes we'll see secondary AML, treatment-related AML, evolve in the setting of ongoing therapy for the primary malignancy or ongoing therapy for a relapse of the primary malignancy, and all of these cases can be quite challenging and need to be managed on a case-by-case, very individualized basis.

Let me outline some of the fundamentals of treatment for newly diagnosed treatment-related AML. As is true with the treatment of primary AML, de novo AML, intensive therapy aimed at inducing a residual disease, negative remission is key. Intensive therapy usually means anthracyclines with high-dose cytarabine or prolonged low-dose cytarabine, similar to what we see in treatment of primary AML. Curing acute myeloid leukemia in the absence of anthracyclines and high-dose cytarabine is exceedingly difficult.

Recently, CPX-351 was approved by the FDA with a label extension for children in the management of secondary AML. CPX-351 has been shown to have an overall response rate of around 80% in children with relapsed AML, not secondary AML but relapsed AML. (The label expansion is supported by safety data from two single-arm trials: AAML1421, conducted by the Children's Oncology Group (COG) and CPX-MA-1201, conducted by Cincinnati Children's Hospital (CCH) and evidence of effectiveness from an adequate and well-controlled study in adults.) We expect that this excellent response rate will extend to patients with treatment-related AML. CPX-351 contains both anthracyclines, daunorubicin, as well as cytarabine, and a liposomal formulation that prolongs exposure to both agents and improves delivery of the molecule to the bone marrow.

If followed, once remission is obtained in these patients, nearly all children will have to go to an allogeneic bone marrow transplant. Though there are reports of cures in patients treated with chemotherapy alone, allogeneic bone marrow transplant remains the standard consolidation

therapy for the management of therapy-related AML. There are other newer agents out there that are not yet approved for children that have been and are being administered under clinical trials, but for now, the mainstay of treatment includes exposure to anthracyclines, cytarabine, followed by bone marrow transplant. Thank you very much for the question.

References

Cooper TM, Absalon MJ, Alonzo TA, et al. Phase I/II study of CPX-351 followed by fludarabine, cytarabine, and granulocyte-colony stimulating factor for children with relapsed acute myeloid leukemia: A report from the Children's Oncology Group. *J Clin Oncol*. 2020;38(19):2170-2177. doi:10.1200/JCO.19.03306

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