
What are the future options for treating older patients who are not eligible for induction chemotherapy?**Amir T. Fathi, MD**

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Welcome to this presentation on the management of AML. My name is Dr. Amir Fathi from the Massachusetts General Hospital. Today, I'd like to discuss emerging options in the treatment of older patients with acute myeloid leukemia who would not be eligible for induction chemotherapy. Typically for this patient population, who are older or who may not be eligible for intensive treatment, we have reserved in recent years the use of hypomethylating agents, which are more gentle, can be given in the outpatient clinic, and generally have a less prominent toxicity profile. This is an important topic because the median age of AML is 67, meaning approximately half of our patients are in their 70s and 80s. Many of these patients may have substantial comorbid burden or may have limited functional capacity or performance status to tolerate more intensive therapies. Hypomethylating agents can lead to response rates in a substantial proportion of patients, although remission rate occurs in a small minority of patients. In recent years, hypomethylating agents have been studied in combination with targeted therapies in subpopulations of patients. In more recent years, there has been increasing interest in the BCL2 inhibitor venetoclax, in combination with hypomethylating agents. Hypomethylating therapies have been combined with the FLT3 inhibitor sorafenib. Sorafenib is FDA-approved for use in certain solid tumor malignancies* and is also a potent FLT3 inhibitor. Therefore, based on results of earlier phase studies, some clinicians do combine sorafenib with hypomethylating therapy for use in patients in FLT3 mutated AML, sometimes in the upfront setting, but the majority of time in the relapsed and refractory setting. Recent trials have also looked at venetoclax in combination with hypomethylating therapy as an upfront strategy in older patients with AML. It is important to mention that venetoclax is not yet FDA-approved for use in acute myeloid leukemia.† It is however, approved for use in CLL and is available. Some clinicians use it off-label given promising data from phase 1 and phase 2 studies. Finally, I would like to mention that in patients who have IDH1 and IDH2 mutations, the use of the IDH1 inhibitor ivosidenib or the IDH2 inhibitor enasidenib as monotherapy is also a rational approach, especially in the relapsed and refractory setting. Thank you so much for listening.

*Sorafenib is not FDA approved for use in patients with AML

† Venetoclax is not FDA approved for use in patients with AML