What would be the best approach to the upfront therapy of IDH1/2 mutated AML among patients who are not eligible for intensive therapy?

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Welcome to *Managing AML*. My name is Dr. Amir Fathi and I'm going to go through some of the questions that I'm frequently asked about the treatment of AML. One question is: What would be the best approach to the upfront therapy of IDH mutated AML among patients who are not eligible for intensive therapy?

We all see older patients or patients who are not eligible for traditional intensive therapy in our practice. The recent approval of the combination of azacitidine and venetoclax for patients with AML who are not eligible for intensive therapy or 75 or older has really transformed our field. I would say that for the majority of patients that we see in our practice, we combine azacitidine or decitabine with venetoclax and have seen good results.

IDH in mutated AML patients also, in theory, have other options. For IDH1 mutated patients, ivosidenib is approved as monotherapy in newly diagnosed patients who are not eligible for intensive therapy. Some people consider using the combination of azacitidine and IDH inhibitors as opposed to azacitidine and venetoclax because of robust data from earlier phase studies such as a phase two study of enasidenib and azacitidine. There are some options there. The question is ultimately, what do I do?

My own personal approach, although my colleagues may have different opinions, is that because of the marked activity of azacitidine and venetoclax in study after study, in IDH mutated patients, in particular, my general approach is to also treat these patients with azacitidine and venetoclax in the frontline setting and leave IDH inhibitors for use if the disease were to progress so that I have something in my back pocket. Mainly because the data around use of IDH inhibitors in the relapsed/refractory setting is also quite good, so we have that option if the disease progresses.

Now would I use azacitidine and an IDH inhibitor in a newly diagnosed patient? Potentially. Azacitidine and venetoclax can be quite marrow suppressive and in a patient who I'm really worried about marrow suppression, I may consider using the combination of azacitidine plus an IDH inhibitor or ivosidenib alone in a person who has an IDH1 mutation.