Why is it important to repeat genomic analysis at the time of AML relapse and what mutation should be tested?

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Welcome to *Managing AML*. My name is Dr. Nicholas Short and I'm frequently asked, “Why is it important to repeat genomic analysis at the time of AML relapse and what mutation should be tested?” This is an important question because we now have approved drugs for various genomic abnormalities that are commercially available. Those would include gilteritinib for FLT3 mutations, ivosidenib for IDH1 mutations, and enasidenib for IDH2 mutations.

Often, we might be inclined to rely on the initial genomic profiling that maybe have been performed when a patient was newly diagnosed and use that to guide the treatment over the course of therapy. It's very important actually to repeat this genomic testing at every relapse because we do see that in a minority of patients, they develop, in particular, FLT3 mutations, but also we can see the development or expansion of new IDH1 and IDH2 mutations in this setting. If these are not repeated, then we might miss the opportunity to treat patients with a targeted drug.

Importantly, in these clinical trials, again, particularly for gilteritinib, we know that outcomes in survival is improved with use of a targeted drug rather than intensive chemotherapy, for example. Very important to repeat molecular testing, certainly at least for those targeted mutations, FLT3, IDH1, and IDH2, and that should be done at every relapse. Now, whether or not it's important to repeat testing for other mutations I think really depends on what other therapies you might have access to in your practice.

If you have patients who you might consider sending for clinical trials, it would certainly be helpful to test for some of those other mutations that are currently being targeted in clinical trials, so that would include also potentially testing for TP53 mutations. We see those develop in about 15% of patients over the course of AML therapy, and now we have clinical trials of magrolimab, which has shown promise. Usually we don't see the emergence of KMT2A rearrangements, those should be present at baseline, or NPM1 mutations. If those were not tested for at diagnosis, they should certainly be tested for at relapse, because we now have clinical trials with menin inhibitors targeting NPM1 mutations or these KMT2 rearrangements.

I would say that the decision about what mutations need to be tested might vary depending on your practice. Certainly, everybody should be tested for FLT3, IDH1, and IDH2 at relapse. If you have access to clinical trials or you often refer patients out to clinical trials, I would also encourage you to do more comprehensive molecular testing so you could identify appropriate clinical trials in your area for that patient. Thank you very much for viewing this activity.

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