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Applying Evidence to Clinical Practice

Announcer:
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Dr. Issa:
This is CME on ReachMD, and I'm Ghayas Issa.

Dr. Fathi:
And I'm Dr. Amir Fathi.

Dr. Issa:
Okay, so we're going to talk about a case that is hopefully helpful for people using these novel drugs, menin inhibitors. So this is a 42-year-old man who presented with progressive fatigue, easy bruising, and epistaxis. His labs show a white count of 22,000, 65% blasts. His hemoglobin was 8.2 and platelet count of 45,000. A bone marrow biopsy showed 75% blasts. And FISH showed KMT2A rearrangement. He had no other mutations detected on next-generation sequencing. So the diagnosis is acute myeloid leukemia with KMT2A rearrangement. He was treated with 7+3 and achieved an incomplete response, or a partial remission. So he was reinduced with FLAG-IDA protocol. And 2 months after FLAG-IDA, he relapsed. At that point, he received the menin inhibitor, revumenib. He achieved an MRD-negative remission by day 28 of treatment. However, during his second cycle, he had prolongation of his QT interval that required a dose reduction, and it resolved with dose reduction. The patient continues on revumenib at the reduced dose, and he continues to be in remission.

So Amir, any comments on how you would approach this case, maybe at diagnosis or at the time of relapse?

Dr. Fathi:
Well, I think this is a fairly representative and successful case of a patient with a very high-risk alteration with AML. As you and I both know, KMT2A translocations are associated with very aggressive presentation and oftentimes refractory just to cytotoxic chemotherapy and a propensity for relapse, so it is an adverse risk alteration in many of our patients. So the fact that this patient thereafter, although achieving somewhat of a response initially, progressed and then relapsed, and then was successfully salvaged with revumenib, is a very reassuring sort of outcome for this case. I hope that the patient continued to respond and did well.

And I would just say that this is kind of what we generally see in patients who have successful outcomes with this, as we know, not everybody responds to menin inhibition, but if they do, generally speaking, it occurs within the first 1 to 2 cycles of treatment. And it is important, I think, to continue to monitor patients over the first several cycles, as patients can develop a response over time. With

differentiating agents, it's not as rapid or predictable in terms of how patients respond. So I think monitoring them over time is important.

The other aspect of this case, which you pointed out, was the QT prolongation. It seemed that that was successfully managed with dose adjustment. It didn't seem that the QT prolongation was that significant or substantial, which is something that you do see that, although there is QT prolongation, oftentimes it's not high-grade and can be managed with dose adjustment, or as needed, dose pausing.

So I think these are the key points that at least I saw in hearing the case.

Dr. Issa:
Yes. And I would add that KMT2A is, like you said, a high-risk or an adverse-risk prognosis AML. So even if during first-line therapy, they achieve remission, I would recommend a stem cell transplant and consolidation. And this is even more true if they had relapsed/refractory disease, and they attained remission on a menin inhibitor, for example, in this case revumenib. This is a young patient, the best chance of a curative intent treatment is a stem cell transplant. What we've learned from menin inhibitors is that when used as single agents, there is a chance of resistance in on-target mutations, so the best outcomes are achieved by doing a stem cell transplant. And a separate discussion would be whether to resume the menin inhibitor and maintenance.

Dr. Fathi:
I agree. And briefly, I just add that there are studies currently planned to sort of look at maintenance following transplant.

Dr. Issa:
Okay. With that, our time is up. We hope you found this case helpful. Thank you so much for listening.

Announcer:
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