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Expert Recommendations and Key Takeaways

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Dr. Fathi:
This is CME on ReachMD, and I'm Dr. Amir Fathi.

Dr. Issa:
And I'm Dr. Ghayas Issa.

Dr. Fathi:
Dr. Issa, can you share your insights with community oncologists on incorporating menin inhibitors into their clinical practice?

Dr. Issa:
So for standard of care, the menin inhibitor, revumenib, is currently approved for relapsed or refractory KMT2A-rearranged acute leukemia, so either acute myeloid leukemia, or lymphoblastic leukemia, or mixed phenotype acute leukemia. And this is really a therapy that could change outcomes for patients with this genetic alteration because frequently, this genetic alteration leads to resistance.

So it is very important for community oncologists, for patients that have relapsed/refractory disease, to check whether they have a KMT2A rearrangement. So these alterations are stable. In other words, if they have them at diagnosis, most likely they have them at relapse. But there could be some nuances that are important to highlight. KMT2A-rearrangement could be picked up by conventional cytogenetics. These would be the common translocations that involve 11q23 chromosome, plus, for example, a common one would be 9;11. But there are instances where the karyotype is diploid normal or not immediately evident that there's a rearrangement, and yet there could be a KMT2A-rearrangement. That's why it's very important to order FISH for KMT2A, which is currently available at multiple centers and should be available to everyone in the community setting. And more and more, we're going to rely on RNA-seq, for example, to pick up these fusions, where there are panels that would allow us to detect KMT2A rearrangements. And this would lead to change in the management and, hopefully, get patients into remission.

Dr. Fathi, anything you would like to add?

Dr. Fathi:
Thank you so much, Gus. I completely agree with you. I mean, I think that some of the topics that we've covered in other episodes of this program also focus on the timeliness of mutational testing, whether it’s with NGS to pick up NPM1 mutations, or with the

cytogenetics and FISH, too. Or fusion assays to pick up KMT2A alterations. There are real practical strategies to sort of identify these patients.

The other aspects of care of these patients in the community revolve around toxicity and management of potential adverse events that may occur while patients are receiving menin inhibitors. There are certain unique class effects related to menin inhibitors, such as differentiation syndrome. This entity is really a manifestation of the mechanistic process of menin inhibitors, the differentiation of leukemic cells into normal cells, that can cause an inflammatory cascade that can ultimately be quite morbid and potentially life-threatening.

So differentiation syndrome needs to be recognized, and it manifests oftentimes as unexplained fevers, pulmonary infiltrates, fusions, rash, adenopathy, but also at times with severe leukocytosis, thrombocytosis, disseminated intravascular coagulation and tumor lysis syndrome. And as suggested by the cascade of symptoms and signs that I've just described, it can be quite severe. So it's important to recognize it. The challenge is it oftentimes mimics other aspects of leukemia patients, such as the disease itself and infectious complications. So if you suspect it, it is important to treat with steroids, to pause the drug to allow the patients to get through this process before resuming the drug.

There are certain therapy-specific adverse events, too, that need to be monitored. The lone menin inhibitor that is currently approved for KMT2A-rearranged leukemias, revumenib, can cause QT interval prolongation, and therefore, this particular adverse event needs to be monitored for closely in patients, particularly those who are on other agents that can also prolong QT.

All menin inhibitors to a certain degree can have the propensity to suppress the marrow, so cytopenias are an issue. Ziftomenib has been associated with rash and itching in a subset of patients. That needs to be monitored closely. There was a signal of nausea that was noted with revumenib. All of these aspects of adverse event management, which, overall, are quite manageable across menin inhibitors, need to be at the forefront of the minds of clinicians in the community that are treating patients with menin inhibitors.

I appreciate this discussion. That's all the time we have today. Thank you, again, for the great discussion, Dr. Issa. And thank you to our audience for listening.

Announcer:
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