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Safety of CDK4/6 Inhibitors: Anticipation, Prevention, and Management of Adverse Events

Dr. Curigliano:

This is a continuous education on ReachMD, and I am Dr. Giuseppe Curigliano.

Today I will review the safety profiles of CDK4/6 inhibitors and discuss strategies for monitoring and managing adverse events.

So we have specific toxicities that are class effect toxicities. Some of them are hematological toxicities, as you know perfectly with palbociclib, and neutropenia is described in 81% of the patients. With ribociclib, we have a toxicity ranging from 69% to 78%. And with abemaciclib, we have less hematological toxicity, with neutropenia accounting for 41% to 46%.

If we move to gastrointestinal toxicity, for palbociclib, we had only 25% of patients complaining for diarrhea. And in terms of liver toxicity, 8% to 9%. For ribociclib, diarrhea is accounting for 29% to 35% of the overall toxicity, but you may have liver toxicity with transaminitis in 15% to 46% of the patients, and QTc prolongation is described in 6% of the patients.

If we move to abemaciclib, diarrhea is the most common toxicity—81% to 86% of the patients are complaining for diarrhea. We have less incidence of liver toxicity, from 13% to 16%. And of note, we have also to remind the risk of thromboembolic events that is more common in combination with tamoxifen.

So when we are going to select a specific CDK4/6 inhibitor in terms of toxicity, we have to remind, finally, that some CDK4/6 inhibitors can be contraindicated in patients with cardiovascular drugs that can prolong the QTc. I mean, I will not give ribociclib to a patient in which the use of a concurrent medication can increase the risk of QTc prolongation, as I will not give abemaciclib to a patient with inflammatory bowel disease.

So the selection should be based on the type of patient you are going to treat. And you have, of course, to increase awareness of patients regarding toxicity in order to have a good management of any side effect.

How to manage abemaciclib-induced diarrhea. If you have a grade 1, of course, with less than 4 stools a day over baseline, you need to continue abemaciclib, and no dose modification is mandatory. Of course, what you need to start is antidiarrheic treatment like loperamide and to increase the oral fluid intake. If you have a grade 2, with 4 to 6 stools per day over the baseline, of course, you need to start antidiarrheic treatment. If you have a resolution within 24 hours and, of course, less than 1 stool a day, of course, you can hold the dose until resolution, and then you can restart again without any dose modification. But if you have a persistent or recurrent at the same dose despite max supportive care, you need to reduce the dose.

For the grade 3, of course, more than 7 stools a day over baseline, you need to stop until resolution, and in any case, you need to reduce the dose. For grade 4, of course, exactly the same attitude. Dietary modification with low fibers, low fat, and smaller frequent meals is mandatory.

Regarding liver toxicity, that is, of course, more common for transaminitis induced by, of course, in this case, ribociclib. For a grade 1, hold the dose until resolution, and of course, you can also resume at the same dose level. For grade 3, of course, you need to obtain that complete resolution. Of course, you can restart at a lower dose, but if you have a recurrent liver toxicity, you need, of course, to

stop the treatment definitively and to consider switching. It's the same thing for a grade 4.

Well, my time is up. I hope you found this overview helpful and thanks for listening.