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Translating Safety Data Into Practice: Effective AE Management in Oral SERD and PROTAC Regimens

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Dr. Kaklamani:
Hello, I'm Dr. Virginia Kaklamani. Welcome to CE with GLC. In this last episode, we will review toxicity patterns for oral SERDs and PROTACs and how we can manage adverse events in our metastatic breast cancer patients.

So when we look at the oral SERDs, we currently have two approved. We have elacestrant and imlunestrant. When we look at the PROTACs, we have one approved, vepdegestrant. But now we have other SERDs that are in clinical trials and may likely be approved in the future, such as camizestrant and giredestrant.

So let's look a little bit at toxicity and, how can we differentiate these agents. Overall, the toxicity profile for these agents is relatively, mild and moderate. Most of the toxicities are going to be grade one and grade two, although in some patients we may have grade three toxicities as well.

When we look at elacestrant, we find some hyperlipidemia, and this is where there's an FDA mandate to actually check lipid profile. Now, this is interesting because it's telling us to check the lipid profile before we start the drug, and then it leaves it under, the discretion of the treating physician as to how often to check it afterwards.

We know this is a class effect, so you may see that the lipids change with other oral SERDs as well. Elacestrant may also have some GI toxicity, some GERD, and some upset stomach, so it tends to be better if we take it with food. Imlunestrant has a relatively similar toxicity profile to elacestrant with some GI toxicity.

Again, relatively mild. So when you look at these agents, they're pretty similar when it comes to their toxicity profile. When looking at the other SERDs, talking about camizestrant here, there's two other toxicities to keep in mind. One is photopsia, and these are flashes of light that happen. They don't seem to have any other issues with vision.

We don't seem to have to take the patients, to send the patients to an ophthalmologist or do any other ophthalmologic exams. But this might be worrisome for some patients and definitely something we need to discuss with them. And there may be some bradycardia, which tends to be all very subclinical. And with giredestrant, we also have some bradycardia, which again, was mostly grade one, very subclinical.

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We don't need to be doing EKGs, but something that you may want to make your patients aware so that they're not surprised if they do find that bradycardia happening. Vepdegestrant seems to be pretty similar to elacestrant and imlunestrant with very mild GI toxicities, but otherwise relatively well-tolerated as an agent.

Now, these are the single-agent toxicities. When we're adding other treatments, such as everolimus, abemaciclib, or other CDK4/6 inhibitors, as you can imagine, we're adding to the toxicities of those agents. And so if you're adding, abemaciclib, you may see a little bit more diarrhea. If you're adding everolimus, you may see some more stomatitis or rash and so forth.

So these are things that we need to be aware of, and this might be able to help us make decisions as to whether to use these agents as single agents or use them in combination. So, I think my time is up. I want to thank everybody for, listening in, and I hope that you found this review helpful.

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