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Interprofessional Coordination of Adverse Event Management

Announcer:
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Dr. Harbeck:
Hi, this is CME on ReachMD, and I'm Dr. Nadia Harbeck. Let's look at adverse event management related to CDK4/6 inhibitors that are given for hormone receptor-positive, HER2-negative early breast cancer and how to manage them. First of all, let's look at the most commonly reported adverse events related to abemaciclib, which is neutropenia about 20%, grade 3; diarrhea about 8%, grade 3; fatigue about 3%, grade 3; and nausea about 30%, but lower grades, grade 1 or 2. I think for the management of our patients, it's important to see at what point of treatment do we have to expect these side effects. Diarrhea occurred early, and the median time to onset was about a week. Incidents decreased over time, and if you look at the higher-grade diarrhea, grade 3, 2 or 3, these events occurred mostly in the first 3 months and had a very short duration of 7 days or shorter, and they did not recur. The discontinuations due to diarrhea were about 5% with the vast majority due to grade 1 or 2 events, and this occurred mostly in the first 3 months. If you look at those patients that discontinued, unfortunately, 75% of them had no prior dose reductions. And I think this underlines the importance of counteracting this side effect early because it's very bothersome for our patients and to keep patients on their medication. And in the trial, physicians and patients didn't know about the efficacy of abemaciclib and now that we know the substantial benefits that patients can expect from this therapy, I think the motivation should be higher to stay on therapy for the whole duration of the 2 years. And our motivation as the treating physicians should be very high to keep patients on that therapy.

The neutropenia occurred a little bit later. The median time to onset was about a month, and febrile neutropenia was extremely rare with 0.3%. The grade 3 or 4 neutropenia was not associated with severe infections and was managed with dose reductions usually within the first 6 months. I think that is important. You do not give G-CSF with neutropenia seen with CDK4/6 inhibitors. The management is holding the dose or dose reductions, and all of these details can be found in the package insert.

I think one of the side effects that's not frequent but clinically important, because also patients ask about it, is venous thrombotic events. We have about 2.5% overall occurrence. About 1% were pulmonary embolisms. And the good news from this study is that less than 1% of the affected patients required hospitalizations. About half of these side effects occurred within the first half year. Most of them did not recur. Management in this study included anticoagulation and dose holds, and discontinuations were low, less than 1%. In patients with a history of a venous thrombotic event, I would definitely choose an aromatase inhibitor as the endocrine partner and not tamoxifen.

With fatigue, I think it's important to note that our quality of life analysis from monarchE showed that there is substantial fatigue in patients in both treatment arms. So we shouldn't forget that these patients had prior chemotherapy; they had surgery; they started with the endocrine therapy. So I think it's important to counsel them regarding this event, that that can happen even after regular breast cancer treatment, not just after abemaciclib, and that we should be patient about that. And once the drug has been discontinued, all of these side effects get better fast.

So what patients have a higher likelihood of requiring dose adjustments? And we know from the detailed analysis that it's those patients of 65 years and older, patients with 4 more comorbidities. And if you look at the data, patients with dose reductions had a lower cumulative dose, but they were more likely to stay on abema. So I think it's important that we really use that mechanism of keeping patients on drug by doing the appropriate dose reductions. Interestingly, older patients do not have more side effects, but they tend to experience higher-grade side effects which need to be managed appropriately.

So with regard to the optimal management of these treatment-emergent adverse events, I think it's important that this management depends on all our team members in the treatment team, be it physicians, be it nursing staff, and given the long adjuvant treatment periods of 2 to 3 years, digital e-health tools will probably become an important tool in managing patients on adjuvant CDK4/6 inhibitors.

In the metastatic setting, for example, we saw in the PreCycle study that the use of an autonomous interactive app where patients' well-being was recorded. And only if that changed and worsened, further questionnaires were put out and patients got a warning saying, please discuss this with your doctor, go to the hospital immediately, and so on. And that can significantly reduce deterioration of quality of life. So it maintains the quality of life, and it significantly also reduces serious adverse events.

So I think what we've learned over the last few years while using abemaciclib and early breast cancer is that side effects need to be managed proactively to keep our patients on drug and that the overall quality of life is not affected by adding abemaciclib, except for the one point that patients are bothered by, diarrhea, which immediately stops once the patient has finished her treatment period.

It is important to use all the measures with pausing therapy until side effects resolve or dose reductions, and after the actual treatment period, there is no long-lasting side effects. In fact, the monarchE side effects after 2 years were actually slightly higher in the control group than in the abemaciclib group. And by talking to our patients, most importantly, I think we should emphasize very early on that dose reductions that become necessary due to side effects do not impact on treatment efficacy. I think that helps patients to be very honest about the side effects early on.

So I hope you'll find this information useful in your clinical practice. And thank you so much for your attention.

Announcer:
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