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Differentiating CDK4/6 Inhibitors in an Evolving European Treatment Landscape for High-Risk HR+/HER2- EBC

Announcer:
Welcome to CME on ReachMD. This episode is part of our MinuteCE curriculum.

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Dr. Harbeck:
Hi, this is CME on ReachMD, and I'm Dr. Nadia Harbeck. During this brief lecture, I'll discuss the CDK4/6 inhibitors that are being used for treatment in hormone receptor-positive, HER2-negative early breast cancer or those that are about to be used.

If you look at the 2 CDK4/6 inhibitors that are available, abemaciclib, which is approved, and ribociclib where approval extension is still pending, they differ with regard to treatment duration, risk stratification and their safety profiles. Treatment duration of abemaciclib and monarchE was 2 years. Ribociclib was used for 3 years. With regard to risk stratification, abemaciclib has very precise indication based on nodal status. It's either 4+ lymph nodes or 1 to 3 lymph nodes with additional high-risk criteria. And in the NATALEE study with ribociclib, a broader definition of high risk was used with basically all node-positive patients and also node-negative high risk, which meant grade 2 and additional high-risk factors or grade 3 tumors.

If you look at the efficacy, it's a bit difficult to compare because abemaciclib and monarchE already presented 5-year data where we saw a carryover effect. So the benefit actually increased with time, and NATALEE only so far showed 3-year data with a small proportion of the patients still being on therapy. But if you look at the hazard ratios, there are rather similar, around 0.7, so it's a very pronounced benefit, although in NATALEE, the data is a little bit earlier.

With regard to the safety profile, with abemaciclib, I think the side effect that's most bothersome for our patients is GI toxicity, it's diarrhea, which we have to manage proactively. Then there is neutropenia, only 20% grade 3, so not that much, hardly any febrile neutropenia and fatigue and some lower-grade nausea. With ribociclib in NATALEE, there was a reduced dose use compared to the metastatic setting. So all of the dose-dependent side effects, such as neutropenia and the QTC prolongation, they reduced compared to the metastatic setting. Liver toxicity, though, remains a problem with about 8% grade 3 toxicity.

With regard to overall survival, there is no mature data yet available for both substances. And I think that's partly also due to the fact that our treatment also for metastatic disease with hormone receptor-positive, HER2-negative subtype has improved substantially over the last few years. Fortunately, patients are able to live for a long time now, even with distant recurrences.

And if you look at the access and reimbursement across Europe, I think there it varies a little. Aemaciclib, though, is standard of care. It's recommended in all the guidelines according to the monarchE inclusion criteria. Some countries only have reimbursement for the clinical criteria, which was about 91%, the so-called Cohort 1 in the monarchE study. And some countries also include those 9% of the patients which had 1, 2, 3 lymph nodes and just a high Ki-67. Ribociclib has not yet been approved anywhere in the world, neither by the FDA nor by EMA. But approval is pending; we expect it. I think then it will also become the standard of care.

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So with both approvals in place in the near future, the differences that become relevant in choosing the respective CDK4/6 inhibitor are obviously treatment duration, some side effects, but I think this choice is actually good news for our patients. And we also have the potential to switch between these 2 CDK4/6 inhibitors if there is any specific tolerability issues. So I think with these CDK4/6 inhibitors, we have now a very good option for high-risk patients in early hormone receptor-positive, HER2-negative breast cancer.

So while this has been a great micro discussion, unfortunately our time is up. Thank you so much for listening.

Announcer:
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