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## Management of HR+, HER2- High-Risk EBC

### Announcer:

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

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### Dr. Mayer:

This is CME on ReachMD. I'm Erica Mayer from Dana-Farber Cancer Institute in Boston. In this brief lecture, I'm going to show how to choose therapy for hormone receptor-positive, HER2-negative high-risk early breast cancer based on current NCCN Guidelines. And I'd like to do that through illustration with a case presentation. So let's get started.

So in general, we've had some really exciting new developments for the management of hormone receptor-positive, HER2-negative early breast cancer, including the use of CDK4/6 inhibitors and the use of adjuvant PARP inhibitor. But how do we put this all together for a patient? So let's explore this in the context of a case.

So I want you to think of this patient, perhaps this is a patient in your practice, and we're going to think about how to put together her adjuvant systemic plan. So let me tell you about her. So this patient is 38-years-old. She's premenopausal. She came into your practice with a 5-cm right breast mass with a suspicious axillary lymph node. Breast biopsy showed invasive ductal carcinoma Grade 2, ER positive 80%, PR positive 30%. HER2 is 1+. And she had an axillary biopsy that was positive. She had early genetic testing and that returned negative for any pathogenic germline mutations.

She received neoadjuvant chemotherapy, dose-dense AC+T, and then she underwent a bilateral mastectomy with an axillary lymph node dissection. Her specimen shows there's residual disease, 3 cm of invasive disease, minimal chemotherapy effect, 4 of 15 nodes are involved. So she has a fairly high burden of residual disease. She is now back in clinic to talk about treatment options. She will be getting her post-mastectomy radiation.

So let's think about her systemic options. Of course, we're going to give her adjuvant endocrine therapy, which for this premenopausal high-risk patient will consist of ovarian suppression and aromatase inhibitor. Because she's young, she may consider oophorectomy at some point.

But on top of that, what type of systemic therapy will you offer her? Here are some choices: Abemaciclib, ribociclib, olaparib, pembrolizumab, a combination.

Think about it for a moment.

In this situation, in addition to our ongoing adjuvant endocrine therapy, I would be picking abemaciclib. This patient meets criteria for the monarchE study. She actually meets it a few ways. She has high-risk disease, she has 4 positive nodes residual after preoperative chemotherapy, she has a 5-cm cancer, and this is exactly the type of person who was involved in the monarchE study. We have mature follow-up data from monarchE showing a defined improvement in invasive disease-free survival that has been growing over time to almost 8%. So this is a drug that works in the adjuvant setting and would be an appropriate choice for her.

You might have been thinking about the other CDK4/6 inhibitor, ribociclib. Ribociclib might not be my choice here, just given the maturity of the data for abemaciclib for high-risk patients. Although, certainly, in discussion with this patient based on the side effect profile, that could be considered as well. So that's our choice for this patient.

Now, let's change her case a little bit. She's still 38. She still presents the same way. But when she has her genetic testing done, it comes back positive. She has a BRCA 2 mutation. And so she moves on with her preoperative chemotherapy. She still has residual disease with 4 positive nodes and 3 cm after surgery, 5 cm originally. So now we're back to our systemic therapy choices. Again, she will get adjuvant endocrine therapy. She will probably have an oophorectomy because of the gene mutation. What do you want to offer her? Abemaciclib, ribociclib, olaparib, pembrolizumab?

Choices? Thoughts?

In this situation, I'm still interested in abemaciclib for her for the reasons that we just discussed. But here, with the BRCA mutation, this brings up the option of offering adjuvant olaparib. We know from the OLYMPIA study that a year of adjuvant olaparib for high-risk hormone receptor-positive patients not only decreases the risk of disease but improves overall survival. Any drug that improves overall survival is a high priority. So in this situation, I want to prioritize offering this patient olaparib.

And so we might think we have 2 active drugs, how do we manage them? Do we give them at the same time? Do we pick the best one? I think in this situation, we can sequence. It's important to remember in monarchE that patients could enter the study up to 16 months after surgery. This means that the patient, your patient, can receive one year of adjuvant olaparib, finish it, and then move on and begin the 2 years of adjuvant abemaciclib.

And so she can get all of the therapy completed within a few years by sequencing it and hopefully get the benefits of both of the agents.

Now, let's change the case again, and this time, still the same patient, same age. She still has a gene mutation, but now she has negative lymph nodes. Her up-front axillary biopsy was negative. She had a sentinel lymph node biopsy at surgery, and it was negative. So she is truly a node-negative patient. Thinking again, what are our choices for systemic therapy? Abemaciclib, ribociclib, olaparib, pembrolizumab.

In this situation, she's node negative. Remember that abemaciclib is only approved for node-positive patients, not node-negative patients. But ribociclib is approved for high-risk node positive and high-risk node negative. This would be a great patient to offer adjuvant ribociclib to. Remember, ribociclib is given at a slightly lower dose for 3 years based on the NATALEE data.

Now, the tricky thing here, though, is what about the olaparib? Can we do the same sequencing that we think about with abemaciclib? In the NATALEE study, patients could enter the study within 12 months of their initiation of adjuvant endocrine therapy. It's a little bit of a tighter window than monarchE, but I think you can still do it and you can give this patient the year of olaparib, then you can transition her to ribociclib for the 3-year course.

That's a lot of therapy to offer this patient, and I think a really important thing to consider here is that if you know you're going to do this, it's important to lay the groundwork early and have your patient prepared. It is definitely a marathon of treatments, but the overall goal is that she gets all the benefit from every single treatment that we can offer to hopefully best optimize her outcomes.

So thank you so much for your attention. I hope this case discussion will be able to help guide treatment selection in your practice. Thank you.

**Announcer:**

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