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Treatment Intensification in HR+/HER2- EBC: Who and When?

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

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Dr. Rugo:
Hello. This is CME on ReachMD, and I'm Dr. Hope Rugo. Here with me today is Dr. Nadia Harbeck. Let's start with a review of the factors that we associate with a high risk of recurrence.

Nadia, can you review those factors with us?

Dr. Harbeck:
Sure. We published that in the current ESMO guidelines late in 2023 where we say, basically, we need to assess the biomarkers, ER, PR, HER2, and Ki-67. And then if in those patients with a 0 to 3 lymph nodes, we can also use gene expression assays for risk assessment and endocrine response assessment.

With regard to the gene expression assays, in the guidelines in Europe, we didn't specify which one, so there's a couple that can be used. The endocrine response assessment is this short-term endocrine therapy before surgery. And then obviously we need the tumor burden of the patient, tumor size, nodal status, number of involved lymph nodes, and grade is something that the pathologists can also give us. And then in those patients with a family history, or if it's therapeutically relevant, which would be in the hormone receptor-positive, HER2-negative setting, patients with 4+ lymph nodes or a non-pCR and a CPS + EG score of 3 and greater, we should also test for germline BRCA mutation.

Dr. Rugo:
And I think the germline BRCA mutation testing is guided there by whether or not you would use adjuvant olaparib per the OlympiA trial. But it's an interesting question, because I find now that with the newer data, that most younger patients are being tested, and quite a lot of older patients in the United States, not just for treatment reasons, but also for the consideration of how we screen, prophylactic surgery, and the implications for family members.

When you're seeing a patient like this, of course we're used to looking at the clinical pathologic features, and that helps us a lot initially. I know that there's a lot of variation in testing for Ki-67. If you know you're going to get a gene expression test, do you think it's worth it to also have Ki-67?

Dr. Harbeck:
Yeah, we do this routinely. In Germany, you get the Ki-67 routinely in the baseline biopsy. But we also do this endocrine response assessment in our patients, because particularly in the young women, that can help us to avoid chemotherapy if a patient has one lymph node has excellent endocrine response, that is after 4 weeks of GnRH and AI [aromatase inhibitors] in the young women's case. And then you have, in the surgical specimen, a Ki-67 of 10% or lower, that's called endocrine response. And those patients, if they don't

have a high risk in a gene expression assay, can then forego chemotherapy based on the ADAPT data. And that's, I think, an add-on which, if you just do the gene expression testing, you don't really get that information, and you may overtreat young women with the biologically more indolent, highly endocrine responsive disease with chemotherapy.

Dr. Rugo:
That's a great point, and I think it is relatively unique. I don't know that that's being used worldwide as a way to decide for chemotherapy or not, and particularly with RxPONDER data that suggested that all premenopausal women benefit from adjuvant chemotherapy.

But how do you manage, then, a patient who has 3 positive nodes and started out with a higher Ki-67? Do you still feel that those patients are candidates for using CDK4/6 inhibitor in the adjuvant setting?

Dr. Harbeck:
We finished recruitment to the ADAPTcycle trial, where we randomized CDK4/6 versus chemotherapy. And I think that can help us decide whom we're going to treat with endocrine therapy, whom we're going to treat with chemotherapy, and whom we're just going to treat with the CDK4/6 inhibitors.

And I think the number of lymph nodes is an important factor at the time being, because the indications for the CDK4/6 inhibitor differ and some for abemaciclib depend on the number of involved lymph nodes. But hopefully in the future, we'll forego that and more look at the biology behind it, and don't count lymph nodes, because in some patients, that may mean that we have to sort of go back in and do additional lymph node dissection, even though for local-regional control, radiotherapy would be sufficient for the patient.

Dr. Rugo:
And that's a really important point, also, that the way we're moving in the future is to really understand the interaction between treatment and individual biologic response, rather than just going in and doing a whole bunch of surgery that creates long-term toxicities that patients can't escape from. So this kind of evaluation, like ADAPTcycle, like the ongoing studies, and even the I-SPY endocrine neoadjuvant trial, I think these are all very important as we move forward. We're testing novel agents and novel combinations.

Thank you for tuning in for this brief discussion. We hope it will be useful for you.

Dr. Harbeck:
Thank you.

Announcer:
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