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High-Risk, HR+/HER2- EBC: Mastering Treatment Selection

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. I'm joined by Dr. Hope Rugo today for discussion on treatment selection for patients with high-risk, hormone receptor-positive, HER2-negative early breast cancer.

Hope, let's start off by looking at prognostic indicators in this setting. What can you tell us?

Dr. Rugo:
This is really an evolving area, Nadia. It's great to talk with you about this topic, because I think it has such a big impact on our decision-making for patients with early-stage, hormone receptor-positive breast cancer. The first information that we get back, of course, is ER. And we know that having high ER versus low ER plays a role. And the recent data looking at immunotherapy in the neoadjuvant setting, also in grade 3 disease, also brought up this factor that really having high ER plays a role in terms of endocrine-responsive versus chemotherapy-responsive disease. Although we don't really understand the cutoffs as yet. We know that an ER less than 10% is important, but once we get into the 30%, 50%, 60%, we're not really sure where the exact cutoffs are.

And then, of course, the other clinical pathologic features. The number of nodes, the tumor size, the grade of the tumor, play a critical role, I think, in understanding prognosis for our patients. And what I think is also really important is that prognosis doesn't necessarily indicate response to treatment. So we really do have to separate those prognostic versus predictive factors in terms of how we decide on treatment. And I think that there are some really interesting data from monarchE looking at Ki-67 that you presented, and we've now published, Nadia. And also, I think, another aspect of this is, can you understand more about prognosis by understanding response to treatment in the neoadjuvant setting?

Dr. Harbeck:
Yeah, I think Ki-67 is an underestimated factor with that regard, because I know in the US, you don't use it as often. In Europe and Germany, we get it routinely. And I think it has 2 values. One is just looking at high Ki-67 and prognosis, and I'll get into the monarchE data in a minute. And the other thing is just to look at the endocrine response assessment. So give the patients 4 weeks of endocrine therapy before surgery, and then look in the surgical specimen whether the Ki-67 is 10% or lower, and that would be called endocrine response. And it’s a very inexpensive assay, and you can actually get a lot from that because you know whether you can rely on that endocrine therapy for the adjuvant setting.

But let's get back to the monarchE. if you look at the two cohorts, cohort 1, which is 90% of the patients, and cohort 2 which is 10%, you can see that the results are qualitatively the same. So there is no difference between the group with the tumor burden as a risk criterion and the Ki-67 as a risk criterion.

So with regard to the role of Ki-67 in monarchE, if you look at the data, you can see it's a prognostic factor; it's not a predictive factor for the benefit from abemaciclib.

In the most recent paper by Dr. Rastogi in *JCO*, it's very interesting. If you look at the high Ki-67 cohort and the overall survival, you can actually see that their hazard ratio is 0.7, and the confidence intervals don't cut the 1. So we've seen in this very, very high-risk population already significant overall survival benefit.

I think we just need to wait and see when the events come in, in the slowly proliferating tumors, and I think then the magnitude of benefit from abemaciclib, it's probably going to increase with time.

Dr. Rugo:
No, I agree. I think that it's been really exciting to see that carryover benefit with a greater benefit when patients have been off treatment now for up to 3 years, where we're seeing an improvement, not just in disease-free or event-free survival, but also in IDFS essentially, but also in distant disease-free survival.

And I think it's important when we're thinking about prognosis and predictive factors, that age does not play a role here. It does predict for more toxicity from therapy, but patients benefit equally, and this has been shown in many settings now, and it's actually really important. We do use our gene expression assays mostly for prediction, but they are also prognostic. So just to mention that patients with higher scores do have a worse outcome with ER-positive disease, in particular, and I think that it's important to keep in mind as we're thinking about these additional adjuvant therapies.

Dr. Harbeck:
Yeah, I completely agree. And I think the story about Ki-67 is still ongoing. I think we've rediscovered this factor sort of as a ballpark estimate about the up-front prognosis. If it's very high, patients usually respond well to chemotherapy and have a poorer outcome overall. If it's sort of very low, then maybe chemotherapy is not such a good idea. But I think the best benefit from measuring Ki-67 is in this dynamic Ki-67 after a short endocrine treatment period.

And with regard to the monarchE data, I think that we've seen that Ki-67 can even be prognostic in such a high-risk population, but it's by no means predictive of the benefit from abemaciclib. So I think we will see the follow-up mature of the study, and then when the events come in in the Ki-67-low population, then probably we'll see the carryover effect mature as well, but time will tell.

So thanks for joining me, Hope. It was a great discussion. But I'm afraid our time is up. So thank you all for listening.

Dr. Rugo:
Thank you.

Announcer:
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