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Case: A Patient With HR+/HER2- EBC at High-Risk for Recurrence

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. With me today is Dr. Nadia Harbeck. Let's start off our discussion with a case.

Nadia, what do you have for us?

Dr. Harbeck:
Yeah, sure. I brought a case where we struggled a little bit with the indication for chemotherapy, but you'll see.

So it's a 52-year-old perimenopausal schoolteacher. She has 2 children, no family history. She self-detected a lump in her right breast, and it clinically was a T2 with 3 cm. Clinically, she was node negative. And we always do ultrasound as well, and she had a G3, ER 100%, PR 80%, HER2 1+, and Ki-67 of 20%. So in our tumor board, we said we really don't know which way this this is going. We have a grade 3, but clinically node negative, Ki-67 20%; that could be good or it could be bad. So let's give her 4 weeks of GnRH plus AI as an induction therapy, and then do the surgery. And as it turned out, at surgery, the tumor size was almost correct, 2.9 cm, but she had 1 involved lymph node, 1 out of 3, and the endocrine response was not present. The post Ki-67 in the surgical specimen was 15%.

So with this no endocrine response, G3, one lymph node, perimenopausal patient, we figured we don't need a gene expression assay, because in the US, you wouldn't test her in that situation. And so we gave her 6 cycles of docetaxel, cyclophosphamide, radiotherapy because she had breast conservation therapy, also to the lymph nodes, and then continue the endocrine therapy, but also offer abemaciclib for 2 years because she had one lymph node and a G3 tumor. And we always do routinely bone density measurements in those women, and also give them adjuvant bisphosphonate.

So I don't know. Do you agree with our management? Would you have done it substantially different?

Dr. Rugo:
Well, it's an interesting question, and I think we've really been struggling with how to manage these patients who have 1 to 3 positive nodes and have some indications for chemotherapy, but we're not 100% sure when they're perimenopausal.

So in the RxPONDER trial in the US, the patients who had 1 to 3 positive nodes who were postmenopausal and had a recurrence score of 25 or below didn't benefit from chemotherapy, whereas the patients who were premenopausal all seemed to benefit, regardless of whether they had a micro met or 1 to 3 positive nodes or a higher or lower score, or any of those things. But only a fraction of patients, under 20%, received ovarian function suppression, which we feel is really important for these higher-risk younger women. And so I think that the issue that's come up is whether or not the endocrine therapy was really the key issue here. And so the OFFSET trial is evaluating that, but it's going to take us many years to get those results. So I do think that we're really faced with this as a complex decision-making process now, as you nicely outlined.

And so I think what would happen in this patient is that, indeed, because she has a positive node, if she went to surgery right away, she would be eligible for chemotherapy as a perimenopausal woman. But there was recently a presentation at ASCO by Kevin Kalinsky looking at the patients who were sort of – where you really don't think they have a lot of ovarian reserve, and they looked at anti-mullerian hormone, and the AMH data suggested that if you really had an AMH suggestive of poor ovarian reserve, that those patients didn't benefit from chemotherapy.

So I think in this kind of situation where somebody's 52, so very close to menopause, we might send a gene expression test to really get that idea, because if they're greater than 25, then they're going to get chemo anyway. Even though we know they wouldn't get a pCR; their rates are very low. But if they were 25 or under, then maybe the AMH would help us a little bit in some decision-making based on that data, which is, again, a retrospective, unplanned subset analysis, but still, I think, quite interesting.

We don't do the induction so much, although in the I-SPY Endocrine Optimization Protocol, we look at the 70-gene score, MammaPrint. And in that situation, if somebody is high 1, sort of low-high 1, node negative, or low risk, they have the opportunity to receive endocrine therapy. We have novel combinations being studied. And we look at Ki-67 and MRI and functional tumor volume, and then if they have a higher score, so they're high 1, high, or node positive, or high 2, then they receive chemotherapy. So that helps us a lot, because we do know that correlates with response at the time of surgery.

And then when we do treat patients in the neoadjuvant setting, we find that the tumor cellularity, along with the Ki-67, can be very helpful in terms of managing and understanding response to the treatment we've given.

But otherwise, I mean, we would definitely offer abemaciclib in this patient. I think she would've been likely to get chemotherapy, as you mentioned, and considering adjuvant bisphosphonates, I think, are very important.

How do you discuss the role of abemaciclib for this patient?

Dr. Harbeck:
Yeah, I think, like you said, we have to separate the question of the chemotherapy from the CDK4/6 inhibitor from the time being, because in monarchE, but also in the NATALEE study, about 90% had prior chemotherapy, so we cannot use those outcome data and say, well, you really don't need chemo; you can take a CDK4/6 inhibitor instead. I think she has a clear-cut chemo indication, because we gave her the optimal endocrine induction therapy, GnRH plus AI, and she did not have an endocrine responsive tumor. And a grade 3 and 1 lymph node being perimenopausal, I think there was just – I love to forego chemotherapy, but in this case, I really didn't see how to do this.

And then we tell her the endocrine therapy worked, but it didn't work in the optimal way, so it's probably good to sort of increase the efficacy a little. And I think that's something that the patients do understand quite well. And then we talk about abemaciclib and talk about the additional 2 years and try to find the right dose very fast so patients aren't bothered by the side effects and can go on with their lives and take that additional therapy. And usually, patients want to protect themselves. I have the experience that they're quite happy to sort of take something if that means that they improve their chances for cure.

Dr. Rugo:
Yeah, I absolutely agree. I think it's all the way we discuss things with patients and helping the patients to understand and sharing together what the goals of treatment are in managing the side effects as well. Managing the side effects proactively plays a really big role.

It's been a fascinating discussion, very quick, but I think that we've hit on the salient points of a really complicated decision-making process that we all face every day. Thank you to the audience for joining us today. We hope that this was also helpful for you in your practice.

Dr. Harbeck:
Thank you.

Announcer:
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