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From Eligibility to Treatment Planning: Translating ESMO Data Into Adjuvant CDK4/6 Decision-Making

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Dr. Graff:
Hi, everyone. I'm Dr. Stephanie Graff. Welcome to CE on GLC Education. I'm a breast medical oncologist, and I'm here today to discuss some of the recent data that's out around adjuvant CDK4/6 inhibitors in early breast cancer and how I'm incorporating them into my clinical practice.

So our case is a 56-year-old woman who has a T2, 3.2-cm, lymph node-negative, early-stage breast cancer. Her disease is lobular, ER 90%, PR 30%, HER2 negative. Ki-67 is 40%, grade 2. Her oncotype recurrent score is sent, and her oncotype score comes back at 26. When we see her in follow-up, she is really hesitant to proceed with chemotherapy, initially refusing chemotherapy with the oncotype score of 26, and is wanting to talk about what the role of oral therapy would be in her care as she weighs that decision.

So I'm sure you've all encountered cases like this where the standard is to proceed kind of with chemotherapy, and you have a patient with an otherwise lymph node-negative hormone receptor-positive breast cancer, and you're trying to figure out how to have those conversations. So first, in my clinical practice, obviously, I would be sitting down and discussing with her how chemotherapy would be the standard of care here.

I oftentimes will do things like look at the RSClin score. In this case, when we run the RSClin score, her 10-year risk of recurrence is 12%, and the absolute benefit of chemotherapy projected is 6%. So that's obviously reducing her risk by half. And sometimes we have those conversations and patients are open to proceeding with chemotherapy after they better understand the details, the side effects of chemotherapy, and how it might inform their risk over time, all the things we can do to support the side effects that they're fearful of.

And sometimes patients are just absolutely not open to getting chemotherapy. So for this patient, let's just assume that she decides that there's absolutely no way that she's getting chemotherapy.

When we dive into the NATALEE and monarchE populations, monarchE only accepted patients that had lymph node-positive breast cancer. NATALEE accepts all patients with positive lymph nodes, as well as patients who are T2N0 and have additional risk factors. And those risk factors include either a grade 3 tumor, a grade 2 tumor with a high Ki-67, or a grade 2 tumor with a high genomic risk profile. This case is potentially eligible for ribociclib based on NATALEE because she has a high Ki-67 and a high genomic risk with a grade 2 tumor that is a T2N0.

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When we kind of dive into the NATALEE data, of course, the intention-to-treat analysis for all-comers did show an improvement in IDFS at the 6-year data that was just discussed at ESMO. It showed a improvement of 5.3% in the 6-year IDFS. That's gradually improved, just like we saw with monarchE. We're seeing that depth of benefit continue to improve as you get farther out in follow-up. I think that this makes sense as we think about the timeline to recurrence in hormone receptor-positive breast cancer.

We'll just see more events the longer both monarchE and NATALEE are followed. Then NATALEE showed us the overall survival data. Again, intention-to-treat all-comers improved overall survival by 2.1% at that 6-year analysis. This is a nominal P value, but statistically significant.

So it's a descriptive analysis. But I think that this really, across the scale of CDK4/6 inhibitor research that we have, across the full portfolio of ribociclib data that is available, I think that this data is clinically meaningful and actionable in how we consider and inform outcomes for our patients.

But for our case specifically, if we sort of dive into those waterfall plots, which is really kind of the subgroup breakdown that's available to us right now for patients on the NATALEE study, we see that patients that are postmenopausal benefit from the addition of a CDK4/6 inhibitor with ribociclib. We see even in the small population of patients who did not receive chemotherapy that they demonstrated a benefit with the addition of ribociclib.

We don't have the specific breakdown of T2N0 or anything like that, but we do have stage II versus stage III, and we see that those forest plots shift to favor the ribociclib. And we have N0 versus N1, and again, we see a clear shift favoring the ribociclib for both of those populations.

For my patient, this case, with a T2N0 breast cancer that has additional risk factors, high genomic risk, high Ki-67, I am going to talk to this patient about ribociclib. She's postmenopausal, so that will be with an aromatase inhibitor. I won't need to add ovarian function suppression here.

As we were discussing this case, this patient has lobular breast cancer. We don't specifically have data from NATALEE about lobular versus ductal in terms of benefit. The things we know are about 17% of the patients in NATALEE have lobular breast cancer.

So again, we go back to that overall intention-to-treat analysis. Patients are benefiting, and 17% is a pretty significant proportion of participants. And I think that if we saw that 17% of the patients weren't deriving benefit, it would have had effects on the larger statistical model.

And so my guess is that lobular patients benefit. We've seen in the monarchE data analysis where more of the translational science has been presented, and they've shown benefit by CDH1 mutations, that those patients also seem to benefit. The presence of CDH1 is probably a loose surrogate for lobular.

We haven't started to see those translational science endpoints come out with NATALEE yet. Given the overall data that we have across the early-stage setting, it likely suggests that all pathologies benefit. The FDA in the United States did do a pooled analysis in the metastatic setting, including the MONALEESA trials that looked at whether or not lobular breast cancer benefited from CDK4/6 inhibitors.

In that pooled analysis, lobular breast cancer patients did benefit from the addition of CDK4/6 inhibitors. And so I think when we look again across the sort of body of work of CDK4/6 inhibitors in breast cancer, there's also compelling evidence that lobular breast cancer patients should be considered similar to the intention-to-treat analysis.

Ultimately, I hope that this case discussion and reviewing some of these high-level data out of ESMO 2026, looking at the 6-year overall survival and efficacy outcomes from the NATALEE study helps you answer some of the questions that you're facing every day in clinical practice.

Thanks for joining.

Announcer:

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