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Recent updates from adjuvant trials in HR+/HER2- EBC

Announcer:
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Dr. Harbeck:
Hi, this is CME on ReachMD, and I'm Dr. Nadia Harbeck. I'm the director of the Breast Center at the LMU University Hospital in Munich, Germany. Today, I will review for you recent updates from the monarchE and NATALEE trials.

Let's start with the 5-year updates from the monarchE, which I had the honor to present last year at ESMO. monarchE, as you all know, is a phase 3, randomized, placebo-controlled trial. It evaluated abemaciclib plus anastrozole, letrozole, or tamoxifen-based endocrine therapy versus placebo plus similar endocrine agents. Primary outcome was invasive disease-free survival. At the 5-year landmark, we saw a sustained benefit of adjuvant abemaciclib in reducing the risk of developing an IDFS [invasive disease-free survival] event. The IDFS Kaplan-Meier curves continue to separate and the absolute improvement in IDFS rates further deepened at 5 years with 7.6%.

The IDFS benefit, I think that's important, was consistent across, across all subgroups. Distant relapse-free survival also was improved by adding abemaciclib to endocrine therapy compared to endocrine therapy alone. At 5 years, the absolute benefit in distant relapse-free survival rates increased to 6.7%, and again, the distant relapse-free survival benefit was consistent across all subgroups. With regard to overall survival, we saw at the interim analysis that there were 7.4% deaths in the abemaciclib arm compared to 8.3% in the endocrine therapy-alone arm. The majority of patients, fortunately, were still alive at the time of this analysis, 84% in abemaciclib arm compared to 81% in the endocrine treatment alone. The data for overall survival is not mature yet. The hazard ratio trends favoring abemaciclib, but that's all we can say at the moment. I think we need to be patient with regard to overall survival because patients do well in the metastatic setting with this type of breast cancer. So I think it's important to wait, but I think the distant relapse-free survival data point in the right direction and show the actual benefit for our patients.

With regard to safety, there were no new safety concerns identified at the 5-year follow-up, and investigators will still collect the SAEs [serious adverse events] regardless of causality. Interestingly, there were slightly higher rates of SAEs observed after the treatment period in the endocrine therapy-alone arm, 7.3% versus 6.5%. I wouldn't make much out of it, but I think this gives us confidence that there is no long-term safety impact. And the safety events observed in the endocrine-alone arm were more infections and GI disorders.

So I think, in summary with the 5-year data from monarchE, we see from the first time a carryover effect for an adjuvant CDK4/6 inhibitor. That's an effect that was first described for tamoxifen, which means that the absolute benefit for patients increases with the follow-up time after the actual treatment period is over. And thus, abemaciclib has become standard of care in high-risk, node-positive, hormone receptor-positive, HER2-negative early breast cancer.

From NATALEE, we have 3-year IDFS data, and here you can see that the risk of invasive disease recurrence or death was significantly lower by about 25% with adding ribociclib to nonsteroidal aromatase inhibitor [AI] compared to the AI alone. The Kaplan-

Meier estimates at 3 years showed about a 3% benefit for ribociclib absolute versus the AI alone. The most frequent sites of distant recurrence were bone and liver, and there was also an effect on distant disease-free survival favoring ribociclib plus the nonsteroidal AI. With regard to overall survival, the follow-up is still rather short, about median follow-up 30 months, and there was 2.4% in the group of ribociclib patients had died versus 2.9% in the endocrine therapy-alone arm. This is a hazard ratio of 0.76, but confidence intervals cross the one, and I think it's too early to tell. Patients fortunately do still very well in the adjuvant setting, and those patients who have a relapse, they also do well in the metastatic setting for quite a while.

At ASCO this year, we saw detailed analysis of the node-negative cohort where efficacy data were rather similar to those in the overall cohort. With regard to safety, the most common adverse events of any grade in the ribociclib group were neutropenia, arthralgia, and liver-related events. And those were also the most common grade 3 or higher events. The liver-related events were the most common adverse events of any grade leading to study discontinuation. So I think the efficacy data of ribociclib in hormone receptor-positive, HER2-negative early breast cancer, very promising. And now we're waiting for the approval extension. Then NATALEE inclusion criteria provide more patients at high risk with an additional treatment option beyond those who qualify for adjuvant abemaciclib, particularly node negative and the patients with 1, 2, 3 involved lymph nodes.

So putting all these data together from monarchE and from NATALEE, I think that with adjuvant CDK4/6 inhibitors, we now have a new, effective treatment option in high-risk hormone receptor-positive, HER2-negative early breast cancer. In NATALEE and monarchE, about 90% of the patients had prior chemotherapy. So we cannot say anything about replacing chemotherapy with the CDK4/6 inhibitor. We just completed the WSG-ADAPTcycle study, which will actually show whether we can replace chemotherapy with a CDK4/6 inhibitor, because that was the primary objective of the trial, and the first results are expected as early as late this year or in 2025.

Unfortunately, our time is up. Thank you for listening. I hope this information will be useful in your practice. Thank you so much.

Announcer:
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