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ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

CDK4/6 in EBC After ESMO: From Early Signals to Greater Clarity

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Dr. Cortés:
Welcome to CE on GLC Education. I am Dr. Javier Cortés, a breast cancer medical oncologist working in both cities, Madrid and Barcelona, in Spain. Today, I will review for you the most compelling data from studies looking at CDK4/6 inhibitors in early breast cancer.

Why do we need this talk? Why do we have to talk about CDK4/6 inhibitors in the early breast cancer setting?

Because we all know that, unfortunately, not all women with early breast cancer will be cured. When we analyze the 20-year risks of breast cancer recurrence after stopping endocrine therapy at 5 years, the data are far from good. The distant disease-free survival is in the range of 78% at 20 years for node-negative disease, about 70% nodes 1 to 3, and roughly 50% for nodes 4 to 9.

It means that a significant number of patients will develop metastasis. And we might say, "Wow, maybe these are coming from old data." Let me look at very carefully the real-world evidence experience, which was presented at ESMO 2024 by Komal Jhaveri. In the node-negative disease, N0, high-risk population, the 7-year distant recurrence was in the range of 13.6%, very similar to the 13.7% in those patients with node-positive disease.

So what does it mean? It means that for high-risk N-positive tumors and also for N0, the probability for the tumors to become metastatic is not small. So we need to do something better. Of course, we have been discussing the role of continued endocrine therapy, but also, we might have incorporate new drugs, and here is when the CDK4/6 inhibitors might play a significant role.

We have four randomized phase 3 trials trying to demonstrate if either palbociclib, ribociclib, or abemaciclib might help our patients. Unfortunately, none of the palbociclib trials achieved the primary endpoint of the study. Both PALLAS and PENELOPE were negative, so palbociclib is not playing today any role in the early breast cancer setting.

However, the other 2 drugs, both abemaciclib and also ribociclib, might improve not only invasive disease-free survival, the primary endpoints of these 2 studies, but also distant disease-free survival. And as we have seen over the last years, also there's a clear improvement in overall survival. So the most important differences between monarchE and NATALEE is basically monarchE explored abemaciclib for 2 years; NATALEE explored ribociclib for 3 years.

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And also, in terms of the patient population, the majority of node-positive disease was included in NATALEE. Not all of these patients were included in monarchE. And also some patients with high risk of N0 tumors were included in NATALEE but not in the monarchE study.

Which were the most important data of these 2 trials?

As I said before, the invasive disease-free survival and the distant disease-free survival was clearly observed in both studies. What is very interesting to highlight is the updated data from ESMO 2026 that we saw in the NATALEE study. In brief, if we remember the data we have, ribociclib given for 3 years compared with nothing, in addition, of course, to endocrine therapy, improved invasive disease-free survival.

And we learned that the distant disease-free survival at 5 years was increased by approximately 3.7%. The distant relapse-free survival was improved by 3.5%. With a 6-year updated analysis, the absolute improvement in distant disease-free survival was 4.9%, and for distant relapse-free survival was 86%.

Also, we had data for the updated overall survival. In this prespecified 6-year analysis, the 6-year overall survival was 91.9% for those patients who received ribociclib. So this belongs to an improvement of about 2.1%.

When we look at the subgroup analysis, it is very interesting to observe that when we analyze the N0 subgroup of patients, the absolute improvement was 2.2% in terms of overall survival. Hazard ratio: 0.79. And it was 0.817 for those patients with node-positive involvement.

So I think that taking into account all this data, in my opinion, ribociclib added to endocrine therapy for a group of patients with N0 by high-risk features of N-positive disease could be considered as another very good option in the early breast cancer setting

Dear friends, dear colleagues, unfortunately, this has been something important to be considered to implement the clinical practice tomorrow, but our time is up. Thanks very much for listening.

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