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

Doublet or Triplet? A Case-Based Debate in First-Line Choices for HR+/HER2- mBC

Dr. Curigliano:
This is CE on ReachMD, and I am Giuseppe Curigliano.

Dr. Jhaveri:
I am Dr. Komal Jhaveri, and we're here today to start a discussion with a case.

We have a 58-year-old Caucasian woman with past medical history for hypertension and hyperlipidemia, and nearly about 7 years ago, she was diagnosed with a stage IIB invasive ductal cancer that was grade 3. Estrogen receptor expression was 90%, PR was 10%, and HER2 was IHC 0. She underwent a lumpectomy, had adjuvant radiation. An Oncotype test was done that revealed a recurrence risk score of 26. She was treated with adjuvant anthracycline and taxane-based chemotherapy, followed by 5 years of adjuvant letrozole.

Now, 14 months after completing adjuvant letrozole, she actually came back to clinic for a follow-up appointment and reported back pain for the past month. A workup to that led to a diagnosis of suspected bone and liver metastases, and biopsy from the liver confirmed metastatic disease from breast cancer, again with ER 80%, PR 0%, HER2 IHC 0.

Next-generation sequencing was performed and demonstrated a GATA3 mutation, an ESR1 mutation with Y537S, and a PIK3CA E545K mutation. Germline testing was also performed and was negative. Other than the back pain, she was otherwise asymptomatic with a good performance status. Her hemoglobin A1c at baseline was 6.8%, and her fasting blood glucose was 140 mg/dL. Her BMI was 27.

So the question here is, how would we think about treating this patient in the first-line metastatic setting? So, Giuseppe, I would love to hear your thoughts.

Dr. Curigliano:
Now, this is a patient, of course, in which you had finally 2 different scenarios that you can select for her. So the first line can be an AI or a SERD plus a CDK4/6 inhibitor versus inavolisib, palbociclib, and fulvestrant eventually. We had the INAVO trial in which, finally, you demonstrated a benefit in terms of median progression-free survival and overall survival. But specifically, what do you believe you would select for this patient? One option, or the other one?

Dr. Jhaveri:
So you reminded us very well about the INAVO120 study. In that study, patients had to recur on or within 12 months of their adjuvant endocrine therapy, so this patient is maybe 2 months off from that cutoff that we consider endocrine resistant. And the hemoglobin A1c cutoff was less than 6%. Fasting blood glucose cutoff was 126 mg/dL.

So they would have not necessarily met the criteria definitively for the INAVO120 study. But I think your point is well taken in the first line with this endocrine-resistant population.

What would the alternate be, I think, if we were to think about this? We certainly have AI, CDK4/6 inhibitors, as you said, that we could utilize. Now, this patient has an ESR1 mutation as well. We think that SERD could be potentially an option.

We have some data from the EMBER-3 trial. Now, EMBER-3 trial looked at imlunestrant compared to physician choice endocrine therapy and also had an arm of imlunestrant plus abemaciclib. And interestingly, that trial enrolled patients, the majority in the second-line setting, but about a third, 30%, were treated in the first-line metastatic setting.

And so technically, if we had this combination available to us at clinic, imlunestrant alone is recently approved, if we were to somehow access imlunestrant plus abemaciclib, one could say, while I optimize the sugars better for this patient, I could potentially even offer something like a SERD and a CDK4/6i based on the EMBER-3 trial as a potential option.

Dr. Curigliano:
So thank you very much. I believe you presented very well efficacy and safety outcomes. Of course, here, this is a first-line treatment. In the imlunestrant trial, there are also later-line therapies that should be considered, but at the end of the story, we need also to consider patient preference when you have treatment that may have potentially the same efficacy.

With that, our time is up, and we hope you found this case-based debate helpful. So thank you so much for listening.