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Released: 12/08/2023
Valid until: 12/08/2024
Time needed to complete: 51m

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Unlocking Insights for Underrepresented Patients: The Role of Real-World Evidence in Addressing Limitations of CDK4/6 Inhibitor RCTs

Announcer:
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Dr. Brufsky:
Hello, I'm Dr. Adam Brufsky, Professor of Medicine at the University of Pittsburgh in Pittsburgh, Pennsylvania. And today we're going to talk about The Role of Real-World Evidence in Addressing Limitations of CDK4/6 Inhibitor Randomized Clinical Trials.

And I think that real-world evidence does give us some more information about populations that are not included in some of the large randomized clinical trials, in particular, African Americans, Asians, and the elderly.

P-REALITY X, that was a large, real-world, first-line, comparative, effectiveness study. And the idea was, is that we went and looked at the Flatiron database, which has about 3 million records in the database already identified, allowing us to examine them. In the Flatiron database, interestingly enough, you know, we were able to kind of take patients from 2015 up until about 2020, and we analyzed a bunch of patients who were postmenopausal women 18 years of age or older with hormone receptor-positive metastatic breast cancer. They had to start their treatment with palbociclib from when it was approved in February 2015 through the 31st of March 2020. And again, the follow-up was either to death, the study cut-off, or last visit. And the planned endpoints were overall survival and progression-free survival. And again, first you can see the unadjusted analysis, and we used two ways of matching the data, inverse probability of treatment weighting and propensity score matching. And I think that's kind of was very well-done trials, been presented multiple times and published recently.

But we had some really interesting subgroups. I mean, the overall patient population did very well. And I think that's been discussed in other of these broadcasts. But what was really important is looking at the African American and Hispanic patients in this. And you can see, there were 37 Hispanic patients in the analysis and 114 African American patients. The unadjusted hazard ratio, looking at palbociclib versus letrozole versus letrozole alone, you can see here in terms of progression-free survival, it clearly is beneficial in African American and Hispanic patients with a real-world progression-free survival of about 20 months on average, versus 7 months with the letrozole alone, a little bit less, I think, than we would have expected.

In terms of overall survival, the same thing is seen here. Palbociclib has an overall survival rate of 12 months of 89%, versus letrozole was 73%, and at 24 months it's 72% of the patients still alive on palbociclib and letrozole, versus 47% on letrozole alone. These are a little bit lower than I think that we've seen in other clinical trials. But again, there may be a lot of confounding variables here; that is, that it could be the Hispanic and African American patients are a little bit of poorer performance status.

What about Asian patients? This is data actually from Korea, looking at Asian patients, and you can see looking at this CONSORT diagram, these are patients that received at least one cycle of palbociclib, when they received, basically, it was about 145 had letrozole

and palbociclib, the majority of the first-line, 24 had fulvestrant/palbociclib. And again, it was basically just following them for progression-free and overall survival. And what you can see here, this is a progression-free survival, there's really mostly progression-free survivals. But you can see the progression-free survival in the Asian patients was about 25 months, which is very similar, I think, to the PALOMA-2 trial and other trials of CDK4/6 inhibitors in the first-line.

When you get to second-line though with fulvestrant, it's a little bit lower, I think, than we would think, it's 6.3 months. And again, these were mostly second- and third-line patients and beyond. So, it's really interesting to see that in the Asian population, this is a little bit worse than say PALOMA-3 and some of the other second-line trials that we have with CDK4/6 inhibitors. The reason for that is unclear, but at least it gives us some information about the performance of second-line agents in an Asian population.

And what about elderly patients? Well, this is data that we actually recently published and was first presented at the Miami Breast Cancer Conference that was recently published, I believe, in *Future Oncology*. And basically, in this particular trial, you can – and analysis, you could see that overall survival the patients 75 years and older, still is higher. This is a little bit difficult to kind of see but the progression-free survival is better in the patients with – on palbociclib. The overall survival was better on the patients with palbociclib in all the analyses, the unadjusted analysis, the inverse probability treatment weighting, and the propensity score matching. So, you can see here everybody did better there.

And there's some other data. This is the POLARIS trial, which is a prospective registry study of about 1,500 patients in United States and Canada. And you can see here in these patients that their global quality of life in these patients over 70 years old, really had no detriment both in the first-line and the second-line. These are patients receiving palbociclib. Their activities of daily living didn't get worse, and their G8 score, which is a score basically about how, again, related to their geriatric assessment and their functional scores really didn't change. And so, this gives us a lot of comfort in that these patients can be treated without really a detriment in their quality of life.

So, I think real-world evidence in special populations helps us understand the role of CDK4/6 in these populations. I think that the hazard ratio is consistent with the randomized clinical trials in most of the scenarios, the absolute progression-free survival benefit, that at least in the first-line, is consistent with the overall trial for both Asians and African Americans, and I think can really be used in shared decision-making.

So again, thank you very much for listening to me and I hope you enjoyed this.

Announcer:
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