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How Does RWE Expand Understanding of CDK4/6 Inhibitor Use in Special Populations With HR+/HER2- Metastatic Breast Cancer?

Announcer:
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Dr. Brufsky:
Hello, my name is Dr. Adam Brufsky. I'm Professor of Medicine and Co-Director of the Comprehensive Breast Cancer Center of the UPMC Hillman Cancer Center Magee-Women's Hospital and the University of Pittsburgh. And today I'm going to talk about how does real-world evidence expand our understanding of CDK4 inhibitor use in special populations with hormone receptor positive HER2 negative metastatic breast cancer?

So these are the real-world evidence that we've used to address populations that were not in the clinical trials. There's male breast cancer, there's cancer in Asians - breast cancer in Asians, and breast cancer and African Americans. All of this are metastatic hormone receptor positive breast cancer. And, again, there were limited amounts or limited numbers of all three of these groups in the large randomized clinical trials, and particularly those of palbociclib.

So this actually involves palbociclib. This is a real-world analysis of palbociclib. In combination with endocrine therapy and men, male breast cancer, again, very rare about 1 in 3,000 of all breast cancers. But this actually was from the pharmacy and medical records database, as well as an electronic health-related database. And you can see here by how these patients are selected, you can start with about 33,000 patients, male breast cancer patients, and again, go down to metastatic disease, and then one cancer type. And as you can see as we go down through here, patients who had palbociclib between February 2015 and April 2017, and suddenly, you're down now at about 147 patients. So the control group, again, there are control groups here. Same thing, you start here with patients who had - male breast cancer patients who had metastatic breast cancer, ICD9 or 10 diagnosis, about 2,000 of these patients. But – and again, you can see you get down to very
small amounts of patients. This is actually the ribociclib instead of palbociclib in this analysis.

And this just shows you kind of the demographics of these patients are pretty typical for male breast cancer. Again, a little bit older than women, a median age of about 64 with palbociclib. And again, the category here about 5% African American, about 3% Asian. Again, all our HR positive, ones that are positive, the vast majority of HER2 negative. And in all of these analyses you can see here, basically most of them had therapy in the first line, although some had the second line.

And because of that, what you see here is that, this is palbociclib alone. This is a mix of first- and second-line patients, the median duration of treatment which corresponds to kind of response is about 9.4 months, was about 3 months with letrozole. So there is a benefit to palbociclib in this particular analysis.

Now, what about Asian populations? This is a real-world clinical data in Asia metastatic breast cancer, these are eight institutions throughout East Asia. And again, I think that East Asian breast cancer is a little bit different. It can predominantly exist in women, be

more of a premenopausal disease, although there are substantial number patients that are postmenopausal in women who habit as well. But what you can see here, these are metastatic breast cancer patients with at least one cycle palbociclib, either with letrozole or fulvestrant. This is women that are postmenopausal, predominantly postmenopausal. And again, predominantly first line going through this CONSORT diagram. And again, looking only at the first-line palbociclib. And you can see treatment is ongoing. However, they do have patients who are on fulvestrant/palbociclib, many of whom have had prior chemotherapy in this particular analysis. So what you can see here is the progression-free survival with letrozole, of predominantly first-line patients. You can see the median progression-free survival is 25.6 months in the Asian population, which is comparable actually to PALOMA-2, with fulvestrant/palbociclib, the median progression-free survival is about 6.7 months - or 6.37 months, which is a little bit less than that seen in PALOMA-3. So at least for the first line, that seems to be about the same. The second line, it's not. And again, if you look back, you can see there's a lot of patients that had prior chemotherapy here. So they were a little bit higher risk, a little bit further progressive, maybe third line even, third line or beyond before they got another hormonal therapy, maybe they had a first-line hormonal therapy, got to maybe one or two cycles of chemo, and then - or one or two regimens of chemo, and then actually received potentially palbociclib in later lines.

This is the best overall response, also similar to that seen in PALOMA-2. Partial response with letrozole and palbociclib seen in about 40% of the patients, a little bit less than was seen PALOMA-2, and with fulvestrant/palbociclib a little bit more actually. The response rate in PALOMA-3 was I believe about probably 15-20% here and in patients with measurable disease. It's about 26-27%. Again, the median PFS is similar to the clinical trial with letrozole and palbociclib, but a little bit less with fulvestrant and palbociclib.

Finally, there was a abstract presented at this year's San Antonio meeting, again looking at the large P-REALITY X experience that we've had with palbociclib from the Flat Iron Database. And again, this is a subset of a trial, a larger trial or larger analysis of about little under 3,000 women treated with palbociclib an aromatase inhibitor or aromatase inhibitor alone, over a about 5-year period from early 2015, to about the middle of 2020. And again, these are the African American subgroups of this particular study. And you can see, again, they're very similar, I believe, to the overall trial itself, median age of AI seems a little bit older, the performance status is roughly the same, just maybe a little bit more patients who have poor performance status, receiving aromatase inhibitor alone. Again, about a third had bone-only disease, looking at the right-hand area. More patients with de novo metastatic breast cancer in this analysis actually received palbociclib. Again, I think the patients with a number of metastatic sites are roughly the same. And the follow-up was a little bit less with the aromatase inhibitor alone.

Of what we can see here from these Kaplan-Meier curves, that there is a progression-free survival benefit. Again, the real-world progression-free survival was 18 months, a little bit less than the clinical trial. But with the aromatase inhibitor, it's about 10 months, also a bit less than a clinical trial. So I think that these African American patients in general, probably had a poor prognosis, so the hazard ratio of 0.63 is close to the hazard ratio seen in the clinical trial of about 0.58.

Interestingly enough in the overall survival, the median overall survival from aromatase inhibitor in the African American population is about 28 months. With palbociclib added to that, it wasn't reached. And again, you know, you have to adjust obviously, the confounding variables here. But there does appear, at least in this limited analysis, to be an overall survival benefit in the African American population is real-world analysis. And again, if you look at the overall survival rate at 36 months with palbociclib, an aromatase inhibitor was about 60 months versus about 44 months with aromatase inhibitor alone. So again, I think that there are benefits in this real-world analysis that are consistent, at least in terms of hazard ratio, with the larger clinical trials.

So I think just to kind of summarize this, I think real-world evidence helps us understand CDK4/6 inhibitors in special populations. I think the hazard ratios are consistent with the randomized clinical trials. In just about all of the scenarios here, they're pretty close in the margins of error. The absolute progression-free survival is consistent with randomized clinical trials in Asians and in African Americans as the absolute PFS difference. And I think these data generally can be used and shared decision-making. I think that, again, they don't substitute for randomized clinical trial, but I think they kind of fill in the gaps a little bit and give us some comfort that when we do observational or real-world analyses, are they are consistent with a randomized clinical trial.

So with that, again, thank you very much for listening to me.

Announcer:
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