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Real World Evidence To Expand Knowledge of CDK4/6 Inhibitor-Related Adverse Effects

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Dr. Gallagher:
Hello, and welcome. My name is Christopher Gallagher. I'm a Breast Medical Oncologist and the Medical Director of Cancer Services at MedStar Washington Hospital Center. And I'm here today with Dr. Adam Brufsky, and we're going to talk about Real-World Evidence to Expand the Knowledge of CDK4/6 Inhibitor-Related Adverse Effects. So, Adam, welcome.

Dr. Brufsky:
Thank you. Thank you very much. Nice to see you.

Dr. Gallagher:
So, in talking about real-world evidence with CDK4/6 inhibitors, we sort of know what the randomized clinical trials say and some of our clinical experience. And what can we learn from some of the real-world evidence about dose modifications and discontinuations, and why they're done?

Dr. Brufsky:
Well, the first thing is, I think the biggest thing people wonder, you know, this is like the old joke that we always used to say, you know, ‘But doc, my hair isn’t falling out, is my chemo working?’ You know, ‘I'm not sick enough, are things working?’ And so, one question people always have is if when we dose reduce, does it really compromise efficacy?

And I think that one thing we've learned, at least across the CDK4/6 inhibitors - let's talk about the CDK4/6 inhibitors, I think those are the most important ones to talk about right now. With the CDK4’s, you know, forever because the progression-free survivals were kind of the same in all the randomized trials and in the real-world evidence, the progression-free survival seems to be the same, you know, basically about 24 to 28 months for most patients, you know, we tended to choose, you know, these based on toxicity. And one of the questions, again, when you do a randomized clinical trial, it's really, you know, everything is closely monitored, and you have to stop patients. You know, if someone had a grade 3 neutropenia, for example, you know, you had to treat them in a certain way, you had to withdraw them in a certain way. If someone had diarrhea, you had to treat them according to the protocol, you couldn't treat them according to your clinical judgment. Hopefully, the clinical judgment and the protocol were the same most of the time.

And I think it's really important, you know, when we look at real-world evidence, to kind of see how these things really work in the real world. A really good example, I think, comes from the P-REALITY X trial. And P-REALITY X was this real-world analysis of almost 3,000 women from the Flatiron database, half of which had letrozole only and half of which had letrozole and palbociclib. And one thing that we found in that database, as well as I think the IRIS database if I'm not mistaken, which is kind of a European and American collaboration, is that the incidence of neutropenia, severe neutropenia, was lower in the real world than in the clinical trial. And there's a lot of reasons for that. I think one reason when we look at a lot of this data, is that you start at a lower dose, I mean, probably 15% of the time or so,

you'd start at 100. American oncologists, interestingly enough, about probably 5 or 10% of them started a patient at 75, which is, you know, really a big dose reduction. But what's really important in that, you know, so that – and so there was lower neutropenia, and it's number one, that's what we saw.

The other thing that we've noticed is that people are always wondering about is the length, you know, is actually data from a long time, are there any long-term side effects by being on CDK4/6 inhibitors? And I think we have the most data from palbociclib. We do have some from abema and some from ribo. But most of it's from palbociclib. And we know, you know, there have been some analyses that have been done of long-term patients on these drugs for three, four, or five years, and really no new side effects have appeared. You know, things like, you know, you're worried about leukemia, or you're worried about some other unknown side effect that could arise. And nothing has happened from that, which is really good.

But I think what also is really important is that we now have data on efficacy in dose reduction, that basically you can reduce the dose and still see the same progression-free survival, which I think is really important across CDK4/6 inhibitors, that we have that data. We have data also from the clinical trials that's helpful. But again, the clinical trials are very controlled trials. And I think in the real world, we tend to dose reduce quite a lot more. We tend to, you know, kind of maybe treat people right at the border or, you know, say a grade 3, you know, reduced to grade 2. I think that when we're in a trial, we're much more conservative about how we treat people.

So, I think that there's a lot of really interesting data that comes out of this, that helps us and helps the patient as well kind of understand that if we have to reduce the dose of a drug, especially a CDK4/6 inhibitor, that they will do just as well and that there are no long-term toxicities. And I think that's what makes patients happy when we kind of talk to them about them and make them feel comfortable about it.

Dr. Gallagher:
Yeah, I agree completely. I mean when you have to tell a woman she needs to be dose reduced, I mean sometimes their first comeback to you is, 'Please don't. I don't want to.' But, you know, when we have real-world data and say, well, it's safe to do it and the efficacy is going to be the same, I think women are very reassured. You know, because there's women who don't want that dose reduction, and I think the real-world data really helps us with CDK4/6 inhibitors and having that conversation.

Dr. Brufsky:
Yeah, I agree completely.

Dr. Gallagher:
Well, thanks, Dr. Brufsky. I think we'll wrap up this part of our conversation. I think it was reassuring to talk about some of the real-world adverse effects and how, when we can measure them, we can actually better inform our patients.

Dr. Brufsky:
Yes, I agree. And again, thank you, everybody, for listening. Thank you very much.

Announcer:
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