Transcript Details
This is a transcript of an educational program. Details about the program and additional media formats for the program are accessible by visiting: https://reachmd.com/programs/project-oncology/how-do-we-implement-annexxa-i-into-our-clinical-practice/16051/

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

How Do We Implement ANNEXXa-I Into Our Clinical Practice?

Announcer:
Welcome to ReachMD. This activity titled How Do We Implement ANNEXXa-I Into Our Clinical Practice? and is jointly provided by Global Learning Collaborative (GLC) and TotalCME, LLC.

Dr. Brufsky:
Hello, I'm Dr. Adam Brufsky, a Professor of Medicine at the University of Pittsburgh, and currently Co-Director of the Comprehensive Breast Cancer Center there. Joining me today is Dr. Christopher Gallagher, who's Medical Director of Cancer Services at MedStar Hospital in Washington, DC. And today we're going to talk about Capturing Value from Real-World Evidence to Optimize Frontline Treatment of Hormone Receptor-Positive Metastatic Breast Cancer.

How're you doing today, Chris?

Dr. Gallagher:
I'm great. Thank you for having me. So, I'm a Medical Director of Cancer Services here, but also practice as a Breast Medical Oncologist. So, look forward to the conversation.

Dr. Brufsky:
Oh, good. Not a problem. So, I guess the real question people have, you know, really when we start talking about real-world evidence is kind of, what is it? That's the first thing. You – what do you think it is? You know, we talk about it versus clinical trials or randomized clinical trials. And so, what do you think? How would you describe it, if you had to describe real-world evidence to somebody?

Dr. Gallagher:
Well, when we compare it to our randomized clinical trials, which we consider our gold standard, when we look at real-world evidence, it's looking at, you know, what are real-world practice patterns? What are patients who receive medications who may not have been included in clinical trials? Whether it was because of comorbidities or their age. And it just really gives us a better idea of how medications are used in patients who weren't included in clinical trials, the ones who would have ended up in our clinic but wouldn't have been in the trial.

Dr. Brufsky:
Right. And that's true. It's just the thing is that we gather the data, you know, not really from randomized trials. So, a randomized trial, you know, is very precise. And you know, you have to have a control group, and you randomize the patients, so sometimes they're blinded, you have no idea what arm you're going to get assigned to. And it's very controlled. And I agree, it's – real-world data tends to be a lot messier. You know, it's us kind of, you know, looking at a large database and are reviewing our own case series or reviewing a large database like Flatiron, and picking and choosing out various patients from them, and then looking at outcomes.

And I guess the question to ask, you know, at this point is, kind of people will say, in the look at it, well, you know, the data look really cruddy, you know, it's like, it's got a lot of problems with a lot of bias and things like that. And, you know, how do we handle that?

Dr. Gallagher:
Well, there's statistical ways that we'll handle it, there's a couple of ways they look at it. One is called propensity score matching and the other inverse probability weighting, which sort of tries to level out some of the bias. I think there's some strengths and weaknesses of both. But I sort of think those two methods complement themselves when looking at real-world data, you know, to give us the sort of the best look that we can.

I agree, there's bias, I mean, without randomization and without, you know, intention-to-treat approaches, you know, it's not something we're used to. And sometimes even the endpoints in real-world data aren't things we're completely used to, whether it's, you know, time to chemotherapy or time to discontinuation of the drug. I mean, some of these things aren't as familiar with us. But I think, as electronic health records expand, and there's more robustness and granularity, I think we'll end up learning a lot of things. And I think real-world data actually can complement some of our randomized clinical trials, and maybe help us close some of the gaps in knowledge, whether it's with safety or efficacy.

But I really think you can also aid in having a conversation with our patients, because they may have questions: 'Does this drug – you know, is it going to be good for me? Because I have these problems, and women in the study didn't have these problems. Like, what does it mean to me?' So, I think it can be very helpful.

Dr. Brufsky:
I think that's really true. And I think that, you know, it's really interesting, I think, what we don't have, and I think what we need, you know, to gain acceptance of this is really kind of the regulatory bodies giving us guidance about what will be used maybe for a label expansion or something like that. And I mean, the reason I think randomized clinical trials are so important, I mean, the science of it is important. But they also were the way that drugs get approved for last 30-40 years, I think the U.S. FDA has really required randomized clinical trials, and randomized clinical trial data, especially in phase 3 trials, to approve drugs. Although I have to say in the incidence of palbociclib, and I think we'll get into that in the next topic, they approved it in men based on real-world data, actually analysis of the Flatiron database.

So, I guess, where this is going, and I think, where the quality of the data and things like that are going to probably become more important, is when we get regulatory guidance, I think, from the FDA, you know, to tell us what's necessary for drugs. I don't think a drug will ever get approved up front based on real-world evidence, but I suspect that drugs will likely get – like label expansions will likely potentially occur based on real-world evidence.

I mean, what do you think? Do you think that's kind of where we're going?

Dr. Gallagher:
I tend to agree. I mean, a lot of times these phase 3 studies, the primary endpoint will be, you know, median progression-free survival. You know, but sometimes when we're comparing drugs, we're looking at overall survival, which wasn't the primary endpoint, but maybe large real-world datasets will help us answer some of those questions and get a better idea. I mean, we have longer follow-up, we have – talk a little bit about P-REALITY X, because that was a large study with over 2,800 patients followed from the Flatiron database, which, you know, interestingly, is mostly a community oncology practice database, so really real-world.

Dr. Brufsky:
Right. No, no, I agree. I mean, I think, you know, now that we even have artificial intelligence, you know, a machine learning to scan these large databases, you know, we may even have more insights that we can get.

So actually, let's turn and let's talk about some of these real-world examples. Do you want to start?

Dr. Gallagher:
Real-world data study looking at palbociclib plus an aromatase inhibitor in metastatic breast cancer, or P-REALITY X, the data came from the Flatiron database, as I said, as mostly community oncology practices. They looked at patients from 2015 to 2020, had 2,888 patients. It's interesting, the median age of the patients that were followed was 70, which is no higher than some of the randomized clinical trials, which is maybe real-world. A fair amount had visceral disease, and they had a follow-up of approximately 24 months. The endpoints they had were, you know, ones we sort of recognize; they had real-world progression-free survival and overall survival. And when using the methods of propensity score matching and inverse probability weighting, when they looked at progression-free survival and overall survival, and they compared palbociclib and aromatase inhibitor to just an aromatase inhibitor, there was a statistically significant improvement in both PFS and OS, which we know from, you know, the PALOMA studies, they couldn't demonstrate OS, but that wasn't the primary endpoint. So, I think it's very interesting that it shows that.

And another study looking at palbociclib was the POLARIS study, which has presented some data. That's a prospective, observational, real-world study where they've had over 1,200 enrolled, and they've had a median follow-up of almost 36 months. You know, and again, it sort of reiterates some of the data from the randomized clinical trials. And I think there's probably more to follow with that one.

But I'll turn to a study with real-world outcomes with ribociclib that was done in Australia, and have a registry called the KARMA registry, which was really designed to look at first-line ribociclib with an aromatase inhibitor in metastatic breast cancer. So, a smaller study, they only had 160 women enrolled and collected data from 2017 to 2018. The women tended to be younger, about a quarter were premenopausal, about a third had visceral disease, and about a third only had bone-only disease, with a median follow-up of about 3

years. And their primary endpoint was this real-world progression-free survival.

And they sort of compared it to, you know, the outcomes in MONALEESA-2, which was one of the, you know, studies that led to the approval of ribociclib. And what they found was progression-free survival in their registry was slightly better than MONALEESA-2, but they really think it was, when they look at the baseline characteristics; women were younger, they had higher rates of bone-only disease and less visceral disease.

So, I think it teaches us something about these real-world studies, you know, we can't control for the biases, we just have to look for the biases. I mean, I think that's what we're going to learn going forward.

And I'll just mention one other study with abemaciclib, the third CDK4/6, it's approved in this setting. And this was a real-world study that looked at claims from a research database where they had 458 patients, the timeline was from 2017 to 2019. And this one was a little more complicated, because abemaciclib was the third one to be approved, so they were looking at patients who either got it with an aromatase inhibitor with fulvestrant, or as monotherapy. And they had very interesting endpoints; they had time to discontinuation of the drug, time to starting chemotherapy, and they also looked at medication adherence and medication wastage, which, you know, maybe surrogates in the real-world data for sort of how the patients tolerate the drug. You know, and the outcomes of that were, you know, for those who did not have a prior CDK4/6, it was very similar to data that was seen in the MONARCH trials, you know, and then when they looked at sort of how that was tolerated in the real world, about a third had a dose reduction within 90 days, but 80-85% or slightly more, remained on drug. So, I think sort of again, it sort of shows us how it's tolerated in the real world.

Dr. Brufsky:
Great. I mean, I think this is all great stuff for people. And, you know, so there are a lot of data out there, I think, that are really important, and really do complement the clinical trials and help us kind of understand that. And I think, you know, we'll spend the last few minutes, you know, talking a little bit about kind of how we can use this data. Clearly, you know, it's clinical trial data, but I think patients really ask, you know, in, you know, shared decision-making. I think that, you know, you want patients to kind of understand what they're getting into.

And I guess the question is, you know, as you said before, I think patients tend to come and they go, 'Well, you know, this is a really good trial, but as you said before, is this going to be useful for me? Are the patients like me in that clinical trial?' I think what the real-world evidence does, is it says, you know, 'Yeah, here are patients like you. Here are patients who are over 75. Or here are patients who are African American. Or here are patients with cardiovascular disease, you know, and they actually did well with the drug. The drug was safe, the drug was, you know, had efficacy, it had a survival advantage.' And I think that's really, really useful.

I think that the patients will trust what we say. I don't think – I mean, do you think patients really care that much whether we talk to them about a randomized trial or real-world evidence? What do you think about that question?

Dr. Gallagher:
I think what they care about is, will they tolerate the drug? And will the drug help them?

Dr. Brufsky:
Exactly.

Dr. Gallagher:
I almost think we're sort of doing some of what we used to do a little bit in reverse, we would look at the results of a randomized clinical trial, and we'd have the patient sitting in front of us and we go, is that the patient who was on the study? Were they postmenopausal? Were they node positive or negative? Were they hormone receptor-positive or negative? And then, you know, now we're sort of seeing patients that have different comorbidities and trying to match them to these large real-world datasets. You know, did they do well if they needed a dose reduction? You know, what percentage needed a dose reduction? How long did women stay on one of these CDK4/6 inhibitors? So, I think we're – the patients are very interested, and I think we can probably have a more informed conversation potentially, when we complement the randomized clinical trial to the real-world data with our patients.

Dr. Brufsky:
Right. No, I agree. And I think that's the most important thing is that we have enough data. You know, as docs, I mean, the patient's in front of us, and it's a unique patient, it's a unique situation. And sometimes, you know, we have that clinical trial data, you know, really very expensive, very well conducted large, controlled trials. But a lot of times, that's not the patient in front of us. And the patient kind of wants to know, you know, and you want to know because you're advising the patient, you know, does this work for that particular kind of patient? I think it's very – that's how the way I think I would look at it to kind of sum this all up, is that we have data now from the real world, you know, in patient subgroups that we didn't have in the clinical trials. And I think it gives me at least a little bit more comfort when I talk to somebody about this.

Do you have any summary comments before we end this?

Dr. Gallagher:
I sort of agree with everything that's said. I would just add, sometimes, you know, when we see the real-world data, it sort of also verifies some of the adverse effects in the real world. You know, we see what happens to some patients on trial, you know, and was there some other adverse effect we were unaware of that sort of emerged. I mean, I think it's just very, again, helpful in having conversations with women that, you know, we're giving them the right drug that we think they should have.

Dr. Brufsky:
No, I agree. Again, I thank you very much, Dr. Gallagher. And thank you all for listening to us on this conversation.

Dr. Gallager:
Thank you.

Announcer:
You have been listening to ReachMD. This activity is jointly provided by Global Learning Collaborative (GLC) and TotalCME, LLC.

To download this activity, go to ReachMD.com/Project Oncology. Thank you for listening.