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

Applying Real-World Data from SABCS 2025 to HR+ HER2- Breast Cancer Care

Announcer:
You're listening to *Project Oncology* on ReachMD, and this episode is brought to you in partnership with AstraZeneca and First Ascent Biomedical. Here's your host, Dr. Pavani Chalasani.

Dr. Chalasani:
This is *Project Oncology* on ReachMD, and I'm Dr. Pavani Chalasani. Joining me to discuss real-world data presented at the 2025 San Antonio Breast Cancer Symposium and its potential impact on hormone receptor-positive, HER2-negative advanced breast cancer is Dr. Virginia Borges. She's a Professor of Medicine and Deputy Head of the Division of Medical Oncology at the University of Colorado Cancer Center, where she also directs the Breast Cancer Research Program and the Young Women's Breast Cancer Translational Program. She also presented on young-onset breast cancer research at the past December 2025 San Antonio Breast Cancer Symposium. Dr. Borges, welcome to the program.

Dr. Borges:
Thank you, Dr. Chalasani. Happy to be here.

Dr. Chalasani:
So, to kick things off, in general, what's the importance of real-world data for oncologists? We see a lot of clinical data coming up more recently—a lot of real-world data being generated—so where do you think the field is going in terms of how real-world data is impacting it or what we are learning from that?

Dr. Borges:
I think the advances in being able to collect these gigantic data sets and interrogate them for outcomes that we otherwise wouldn't have is shaping our field in ways that are important. Obviously, we always want to make the major practice-changing decisions and define our guidelines on the results of level one evidence or randomized clinical trials.

As we all know, we often get into the situation where trials have been run and resulted in parallel, and then there isn't an easy certainty of the tie-in of how we marry the results of one study versus the other—or, if we have two advances that come out at the same time, which takes priority. Also, while we have these results of our clinical trials and we have our guidelines, we don't actually know what happens in terms of what then transpires when this is rolled out into what we have to do—as the saying goes—on Monday morning in the clinic. How easy is it? How realistic is it? How acceptable is it to our patients to then deploy all of these new advances and guidelines?

And so what I have found most impactful about the real-world evidence is being able to get out the microscope and see what we are all really doing collectively as a field and where gaps are in what is happening as a field that we could identify, and then making sure that we are investing in improvements so that our patients are benefiting from all of the time, effort, and expense that goes into these huge clinical trials and the advances that are made. And then also, how do we fill in the data-free zones? What do we do in the later line settings? All the new advances often come in the first or second-line setting if we're talking about metastatic disease. Or, if we have a new advance in early breast cancer, what do we do now in first-line metastatic disease if we've moved drugs up in the pipeline?

So that's kind of how I look at it with the real-world evidence we have on hand now.

Dr. Chalasani:
With that in mind, what were some of the most practice-relevant in-the-world findings related to hormone receptor-positive, HER2-

negative advanced breast cancer that you saw presented the past year?

Dr. Borges:
If we look specifically at San Antonio—which just happened a month ago and is often where we see some of the most important breast cancer outcomes data coming—what I thought impressed me the most in the real-world evidence space was a presentation regarding the Flatiron Health Database, where the investigators went back and did an analysis of how often patients were getting tested for the emergence of an *ESR1* mutation when then they and their clinician were deciding what was going to be the next line of treatment.

So we know that *ESR1* is, of course, something that emerges in the face of previous hormone-targeted therapy as an escape mechanism. And we now have two drugs that are FDA approved specifically for our patients who have developed one of these *ESR1* mutations: elacestrant, which we've had for a couple of years now, and then just recently, we've gotten FDA approval for imlunestrant.

So we have two opportunities for our patients to be able to target something that is a driver escape mechanism of their cancer. But if they're not getting tested for it, then there's no way they're getting these new meds, which one could interpret as a concern that they're being bypassed of an opportunity that could benefit them. This will likely result in them ending up on infusion therapy, which, while those are drugs that work well for our patients, we all know that we want to push that off as far as we can safely for our patients by employing these more targeted therapies first.

Dr. Chalasani:
So, just to follow up on that, we are getting more treatments. How do you see these real-world insights shifting treatment selection?

Dr. Borges:
I think when we see real-world evidence like this, it's a bit of a wake-up call. And hopefully, it allows all of us to go back to our practice and say, "Why am I missing this?" or, "Am I missing this?" And also, these are opportunities, right? We can talk about it. We can remind folks that this is an important thing to do, particularly now that we have two drugs that somebody could choose from for their patient. And I think there will be more to follow, as there are ongoing clinical trials that we are getting the results of and going to continue to get the results of in the next few years.

This is an emerging space. People really need to get their brain around the logistics of repetitive testing, which is new in breast oncology. That wasn't something we used to do.

Dr. Chalasani:
For those just tuning in, you're listening to *Project Oncology* on ReachMD. I'm Dr. Pavani Chalasani, and I'm speaking with Dr. Virginia Borges about real-world evidence on managing hormone receptor-positive, HER2-negative advanced breast cancer from the 2025 San Antonio Breast Cancer Symposium.

I would like to get your thoughts on a few specific areas of interest that were presented at the symposium. The first is on CDK 4/6 inhibitor use. Was there any real-world data that stood out to you regarding when or how to best use these agents?

Dr. Borges:
There was one study that I liked. It was a real-world comparison of frontline CDK 4/6 inhibitors, including all three of the currently commercially available ones: abemaciclib, palbociclib, and ribociclib. And what that real-world evidence showed us was that it didn't really matter which one you picked. They did not see a clinically significant difference in the overall survival, which was averaging at 30 months, independent of which agent was chosen in the real-world setting.

And why we care about that is, as we get the results of one clinical trial, then the results of another clinical trial, and the results of a third clinical trial, we're not supposed to compare across clinical trials, yet we always do. And there can be differences in the length of the progression-free survival for the novel drug—the CDK 4/6 inhibitor being added to the backbone of the endocrine therapy—and also, we saw in the original three frontline clinical trials of these agents that there was a difference in which ones showed overall survival versus not. There were a lot of differences in who got enrolled on those clinical trials in terms of prior treatment, use of chemotherapy, and de novo percentage versus recurrence out of having previously been treated in the early breast cancer setting. And so it was always a little bit hard to know if there was a difference between these three or if it was just happenstance of what can occur across multiple clinical trials.

Now that we've seen it really rolled out there into the real-world setting, it looks like it is dealer's choice as to which they could opt to offer one of their patients.

Dr. Chalasani:
Changing the topic slightly, were there any insights that were particularly exciting for you in real-world evidence on treatment disparities or cancer care disparities at the symposium?

Dr. Borges:
So we did see some data. I guess exciting isn't quite the word I would use to describe it, because any time we can identify the persistence of some of the biases that exist for our patients that can be identified based on who they are or who their ancestors were on this planet—I find it disheartening that in 2026, this can still be identified. But it is important from real-world evidence for us to see what is happening and therefore identify opportunities for improvement in our own practices and as a community.

So there was some real-world evidence that did highlight that women who are Black or Hispanic and getting diagnosed with metastatic hormone receptor-positive breast cancer did have a significantly longer wait time in comparison to patients who were White being diagnosed in the same instance. And what was nice about this real-world evidence is they did figure out a way to control for some of the socioeconomic factors that you might think could have played into that. So it doesn't seem like it was the opportunity of the patient to be able to afford the copay or get the medication due to socioeconomic reasons. And so why do we see that? What does that actually mean? Is there an inherent bias that these patients are not being given the level of priority that another patient might be in terms of getting the prescription in, getting it approved through the insurance, getting it out to the pharmacy, and making sure they have it on hand and are taking it in a timely manner?

It wasn't a big difference when you look at the number of days, but it did meet statistical significance. And while, ultimately, it probably wouldn't change that patient's ability to benefit from the medication—because we're talking about first-line metastatic treatment, where a few days is unlikely to make major difference—it shows us this pattern. And we could envision that there are other circumstances in patients' care where this pattern could impact their ability to benefit from their treatment if they were more ill.

We do know that we can use CDK 4/6 inhibitors and endocrine therapy in the frontline setting, even if there is a lot of visceral disease—even visceral crisis from some of the previous clinical trials that we have seen. So if it was one of those patients, it could potentially impact how soon they're going to benefit and whether or not they're going to get into trouble before that benefit kicks in.

So, again, it's a little bit of a real-world evidence wake-up call for us as a community to focus on how we can make sure this is not what is happening in our clinic on Monday morning.

Dr. Chalasani:
As we come to the end of our program, Dr. Borges, what's one key takeaway from the San Antonio Breast Cancer Symposium that you think should influence clinical practice right now?

Dr. Borges:
We did see quite a few data from some of the practice-changing trials that came out that is important for estrogen receptor-positive metastatic breast cancer. We did get data demonstrating that elacestrant can be combined with abemaciclib. This was phase 2. But it did show a progression-free survival of 14.3 months and a very high disease control rate in over 90 percent of the patients.

We also saw that in an analysis of giredestrant plus everolimus, there was a significant improvement in progression-free survival compared to just endocrine therapy for patients who had previously had CDK 4/6 inhibitors. And I like that data in particular because I think everolimus has become a little bit of a forgotten drug that many patients can still benefit from. Again, it's an important situation where you want to be testing for that *ESR1* mutation if you're not going to be combining it with a SERD, given some of the resistance patterns we know of from previous data.

We saw updated results from SERENA-6 with camizestrant and the role of doing circulating tumor DNA, looking at whether that will help us identify the emergence of the *ESR1* resistance prior to progression. I will admit I have not yet adopted that as a standard practice in my clinic. I'd like to see, maybe, a different study with a different randomization schema, where it was a little bit more of a direct comparison. But it is giving us the knowledge that these tools are coming, and it probably won't be too long before we will have a deep understanding of how to really get them into our clinical practice. And how lovely would it be if we could just do blood tests and not have to send patients for scans all the time? It's sort of a hope.

We also saw exciting data from EMBER-3 that we got extended PFS for the combination of imlunestrant and abemaciclib. We don't have that partnering FDA approved yet, but imlunestrant is available, as is abemaciclib. So we have safety data and PFS beyond monotherapy with just imlunestrant.

And of course, what was unfortunately not a positive trial was the ASCENT-07, where we saw that sacituzumab govitecan moved into the first-line setting of IV therapy after endocrine therapy did not outperform standard-of-care chemotherapy, which I think was a little surprising given that we had seen such benefit in the second-line setting for sacituzumab.

So those were some of the big takeaways for metastatic disease for me from the conference.

Dr. Chalasani:
That was a great summary. As we wrap up today's program, I want to thank my guest, Dr. Virginia Borges, for joining me to discuss ways real-world findings are influencing treatments for hormone receptor-positive, HER2-negative advanced breast cancer. Dr. Borges, it was great having you here today.

Dr. Borges:
Thank you so much, Dr. Chalasani. I really enjoyed our time.

Announcer:
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