Transcript Details
This is a transcript of a continuing medical education (CME) activity. Additional media formats for the activity and full activity details (including sponsor and supporter, disclosures, and instructions for claiming credit) are available by visiting:
https://reachmd.com/programs/cme/from-abstract-to-action-in-breast-cancer-interpreting-recent-data-on-oral-serds-and-endocrine-targeting-strategies/57230/

Released: 07/22/2026
Valid until: 07/23/2027
Time needed to complete: 37m

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

From Abstract to Action in Breast Cancer: Interpreting Recent Data on Oral SERDs and Endocrine Targeting Strategies

Announcer:
You're listening to GLC on ReachMD. This activity is provided by Global Learning Collaborative and is part of our MinuteCE curriculum.

Prior to beginning the activity, please be sure to review the faculty and commercial support disclosure statements as well as the learning objectives.

Dr. Bardia:
Hello from ASCO 2026. Today, we'll discuss some of the most important breast cancer data presented at ASCO, involving oral endocrine therapies as well as combination with targeted therapies, and what they mean for clinical practice.

I'm Dr. Aditya Bardia, medical oncologist at UCLA. With me today is Dr. Erica Mayer.

Dr. Mayer, ASCO 2026 featured several important updates involving oral SERDs as well as combinations. Broadly, what themes stood out for you this year regarding the evolving role of oral endocrine therapies in ER-positive breast cancer?

Dr. Mayer:
Thanks so much for having me, Aditya. I'm really excited to be here and talk about this exciting category of medications.

So this year's ASCO was really interesting, looking at a variety of different trials exploring oral SERDs. Up until now, most of the data we've seen has been in the pretreated setting in patients who've already had first-line therapy with endocrine therapy ± a CDK4/6 inhibitor. This year at ASCO, we've begun to see more data moving oral SERDs up into earlier stages of treatment, for example, in the first-line setting in the trial or in the, shall we say, 1.5-line setting in the SERENA-6 trial, and including more follow-up from the pretreated settings, such as the evERA trial.

We've also seen oral SERDs make it into the early-stage setting, as you know well, and excited to hear more data about the maturity in that space.

Additionally, at ASCO, I think we've seen more data and more thinking about how we identify candidates for oral SERDs, in particular looking at the molecular characteristics that help us understand who our best candidates are, and this includes identification of the emergence of *ESR1* mutations, looking at other co-mutations, and also thinking about specific populations and how they respond to oral SERDs, including both pre- and postmenopausal patients.

So a lot of new data has come in, and ASCO is really helping us dig into the existing trials and emerging trials of oral SERDs to really help us better understand how we deploy these agents and in whom.

© 2026 ReachMD

Dr. Bardia:
Yeah, absolutely. It was good to see the oral SERD data continues to have a place in the second-line plus setting as single agent with elacestrant and imlunestrant, and then potentially combination therapy that you presented last year, Dr. Mayer, giredestrant plus everolimus, and a biomarker data that looked very exciting. So that's another potential combination.

But if you go to the first-line—you alluded to this—we saw the persevERA data looking at giredestrant plus palbociclib versus AI [aromatase inhibitor]/palbociclib. Overall, the study did not meet statistical significance, but there was a trend towards improvement in median PFS. Your thoughts about that study and the role of oral SERDs in general in metastatic breast cancer?

Dr. Mayer:
Yes, that was a really interesting presentation, very thought-provoking for all of us.

So the narrative prior to seeing persevERA data is that the greatest benefit of an oral SERD appears to be when the cancer has developed an *ESR1*, or estrogen receptor, mutation that can lead to resistance—endocrine resistance—and we've seen that theme in the monotherapy studies and some of that also in some of the combination trials.

Moving into the first-line setting, persevERA enrolled patients who were endocrine sensitive. They were randomized to aromatase inhibitor and palbociclib, or giredestrant and palbociclib. And in that first-line setting, we would actually expect the prevalence of *ESR1* mutations to be quite low, so quite different than other oral SERD trials that we've seen so far.

And as you point out, there was this sort of interesting trend in the PFS curve. Officially, it was a negative trial, no substantial difference between the arms, but for the first 12 to 16 months or so of treatment, the curves were overlapping, and then they began to separate. And we do know that around that time, about a year or so into treatment, is when we really do see the emergence of these *ESR1* mutations.

So are we seeing that biologically these cancers are developing the mutation, and then we see the differential benefit from the different medications? I think it's a really interesting theory. We'll need to wait for more molecular data from this trial, particularly about *ESR1* status at baseline and onward, in order to understand if that really is in play.

I also think it's interesting that this is a study using a combination with a CDK4/6 inhibitor in the first-line setting, a setting where we know that CDK4/6 inhibitors have a very prominent effect, have tremendous efficacy, and it may be that by adding in the CDK4/6 inhibitor, the differential benefit of the endocrine partner may become less apparent. We actually saw this from the PARSIFAL study years ago, which randomized patients to aromatase inhibitor or fulvestrant, both with palbociclib, and saw no substantial benefit between the arms.

So I think the data is really quite interesting and does not necessarily dampen enthusiasm for oral SERDs but just develops the story of who are these agents for and when is the right time to deploy them.

What was your take on that data?

Dr. Bardia:
No, I fully agree, and especially after 12 to 18 months, that's where you start to see separation of the curves, which is a good segue into *ESR1* mutations.

And in SERENA-6, in that study, the question is, when you have *ESR1* mutation that's detectable in the blood, but patients do not have radiological progression, switching to camizestrant showed an improvement in progression-free survival, progression-free survival 2, as well. We saw updated data at ASCO that clearly showed improvement in progression-free survival 2. Previously, we've seen improvement in quality of life as well, delaying the use of chemotherapy.

We'd all like to see overall survival data. And if overall survival is improved by the early switch, I think there'll be no questions asked that that's the approach that should be taken. But if you don't see overall survival, that's where it gets a bit tricky. But biologically, it's very appealing to look at *ESR1* mutations and, at the time that *ESR1* mutations are present, make a switch to an oral SERD.

© 2026 ReachMD

The challenge is also practical in terms of how frequently do we monitor for *ESR1* mutations. What's the cutoff and the clinical relevance of this serial ctDNA monitoring? We've not done that in clinical practice, so this will be a game changer in terms of adoption of this in the first-line setting, looking at *ESR1* mutations and then making a switch like we do with a tumor marker, and the adoption not just in the academic setting but the community setting as well.

And if you have additional thoughts, Erica, regarding SERENA-6 and this whole idea of molecular monitoring and progression.

Dr. Mayer:
Yes, I think SERENA-6 is one of the most innovative clinical trials we've had in the breast cancer space in quite some time. Asking questions about how we test, what are we looking for, what do we learn about tumor biology, and what is the efficacy of a specific drug. So there's really many facets of breast cancer care and biology that are being addressed by the trial. In some ways, though, that makes interpretation of the trial and its results really more complicated for all of us.

The recent presentation at ASCO, I think, was very helpful. With greater maturity of the data, we see the PFS benefit is preserved. In fact, it's interesting, at like 3 years of follow-up, 1/3 of patients have not progressed, the ones who were randomized to receive camizestrant in that trial. So there's a preserved and stable PFS benefit. We see the PFS2 benefit. There's a delay in time to chemotherapy, which I always think is really clinically meaningful for patients.

And there was really interesting data presented, looking at ctDNA itself and showing that in the 2 arms of the study, about 1/2 of the patients had cleared their ctDNA with camizestrant by 2 months into the trial, compared to like 2% of the patients in the control arm who did not switch their therapy. And of the patients who completely cleared ctDNA, this was totally an exploratory analysis, but they actually had an improved overall survival compared to the other patients. So very provocative and an interesting way of looking at ctDNA dynamics.

Now, taking all of that and bringing it into clinic is something for us to think about. In essence, the ctDNA frequency is checking it 4 times a year; it's every 3 months, and many of us are doing our scans on patients 4 times a year. So when I've thought about doing this, I think about maybe sending the ctDNA 2 weeks before a scan because it takes a little time for it to come back, and then when you're sitting down with the patient reviewing the scan results, hopefully you have that ctDNA result with you, and either it all looks good and you carry on with your therapy, or if you are in that situation of emergence of a mutation without clinical progression, that's the time then when one could bring up the idea of switching therapy.

I think it does require making a little change in the way that we assess patients and the timelines and how our clinic staff help us get this set up. It also will require us learning how to talk about this information with patients and how to explain what it means in a way that, hopefully, will focus on that this is helpful and this is going to help people do better and not be something that would create anxiety for our patients.

I will say I think patients really like getting the data from ctDNA. I think it's nice to learn as much as we can about cancers. So my suspicion is that people will welcome getting extra information, but we need to be really careful about how we educate ourselves and our patients about communicating this type of data.

Dr. Bardia:
Well, that's great, Erica. That was very practical, helpful, and [showed] how to incorporate this in clinical practice. We'll always need more education, but it's moving in the right direction with these molecular assays. So we await the FDA decision related to camizestrant and SERENA-6 and our exciting times ahead.

We've covered a lot of exciting developments today, from endocrine therapy evolution to biomarker-driven strategies. We talked about oral SERDs, the space second-line plus, 1.5, and then also the persevERA study. So before we close, let's bring this down to the practical level. Erica, if you had to identify 3 top oral SERD-related takeaways from ASCO 2026 that might influence clinical practice, what would those be?

Dr. Mayer:
I think some of the top data that I saw at ASCO, some of which we've already touched on, so I do think that SERENA-6 is something that all of us need to keep paying attention to and waiting for the FDA decision, seeing if this does become a paradigm that enters our

© 2026 ReachMD

practice.

I thought the persevERA data, which I think we were all really waiting to see, was very informative and very thought-provoking.

I will add, I also really liked seeing the follow-up evERA data. evERA is a combination study using giredestrant and the oral mTOR inhibitor everolimus post-CDK. And we saw that in that trial, not only do we have the positive PFS in the ITT and *ESR1*-mutant population but also, for the first time, positive PFS2 and delayed time to chemotherapy, again an important clinical endpoint.

And we are continuing to see very interesting data from the ELEVATE study, which is a multi-cohort phase 1/phase 2 study that's looking at the oral SERD elacestrant in combination with targeted partners. We've already seen data looking at elacestrant with a variety of CDK4/6 inhibitors, and right now we are beginning to see data with capivasertib, the AKT inhibitor.

Phase 1 data was presented that demonstrated that the agents were well tolerated together, like we've seen with other oral SERD combinations. The toxicity profile is as we would expect for giving fulvestrant with capivasertib. There's no synergistic toxicity when we add elacestrant and capivasertib, which is very reassuring. And a little early for efficacy data, although the sample size is still a little too small to have robust data there.

So that was very reassuring and certainly would be a nice type of option for patients with dual mutations, where they have both an *ESR1* mutation and a PI3 kinase pathway mutation, and you're looking for a combination that might target both of those strategies.

So I thought those were really helpful data. I'm not sure anything is ready for clinic tomorrow, but definitely data that continues to build this very nice narrative about the role of oral SERDs.

How about you? What did you think about some of the trials at ASCO? Particularly, I always like trials in progress to see kind of what's coming down the pike for us.

Dr. Bardia:
Yeah, no, absolutely, I fully agree, and elacestrant was the first oral SERD, the poster child in terms of oral SERDs. And so in terms of trials in progress, there are a number of studies looking at elacestrant in combination and also in early breast cancer. So, for example, the ADELA study is looking at elacestrant plus everolimus versus elacestrant plus placebo in the second-line plus setting for patients who have *ESR1* mutations. Elacestrant is the standard of care in that setting. So this trial is asking the question, if we add everolimus similar to the evERA trial, would that improve outcomes?

Similarly, the CAPELA study is looking at elacestrant with capecitabine versus capecitabine in ER-positive metastatic breast cancer. Elacestrant is also being combined with abemaciclib for patients with brain mets, an unmet need in ER-positive HER2-negative breast cancer. In general, we don't see a lot of brain metastases in ER-positive setting, but when seen, that can be associated with worse prognosis, and since abemaciclib and elacestrant cross the blood-brain barrier, this trial is looking at the combination of these 2 active agents.

And then finally, in early breast cancer, the ELEGANT study is looking at elacestrant in the switch strategy, meaning that when patients have received at least 2, up to 5 years of endocrine therapy in the adjuvant setting with/without a CDK4/6 inhibitor, randomization to continuing the same endocrine therapy, AI or tamoxifen, versus a switch to elacestrant in this setting. So it'll be good to see data from these trials, as they would further refine clinical practice regarding the use of oral SERDs.

So this was great. Before we wrap up, Erica, do you want to provide us 1 key takeaway from this activity?

Dr. Mayer:
Well, I think a key takeaway about oral SERDs is for decades all we've had was tamoxifen, aromatase inhibitor, and then fulvestrant, and honestly, for my whole lifetime as a medical oncologist, that's what I've had. And now we're going to have this new category. I mean, we already have it, but the new category of oral SERDs is going to penetrate every aspect of breast cancer care for hormone receptor-positive disease: pretreated patients, I think eventually first-line patients, early-stage patients. And these are well-tolerated drugs, highly effective, and they mix well with all of our favorite targeted partners.

© 2026 ReachMD

So I'm envisioning a future for us where these agents really become our preferred selection for patients. So it's really exciting to see all of the data coming out and thinking about how this will step by step change our practice, but there's a lot of trials to pay attention to, so I'm looking forward to continuing to do this together with you.

How about you? What do you think your big takeaway is?

Dr. Bardia:
Absolutely, oral SERDs are slowly replacing AI and tamoxifen, so they've been becoming the preferred endocrine therapy partner in the metastatic setting, and likely we'll see this in early breast cancer as well.

Excellent. So that's all the time we have today. I want to thank our audience for joining us. Thank you, Erica, for sharing your expertise, your insights. It was great speaking with you today.

Dr. Mayer:
Thanks so much. Take care, everybody.

Announcer:
You have been listening to GLC on ReachMD. This activity is provided by Global Learning Collaborative and is part of our MinuteCE curriculum.

To receive your free CE credit, or to download this activity, go to ReachMD.com/CME. Thank you for listening.

© 2026 ReachMD