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/spotlight-on-serds-for-erher2-advanced-breast-cancer-what-clinicians-need-to-know/14791/

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

Spotlight on SERDs for ER+/HER2- Advanced Breast Cancer: What Clinicians Need to Know

Announcer:
You're listening to *Project Oncology* on ReachMD, and this episode is sponsored by Stemline, a Menarini Group Company. Here's your host, Dr. Jennifer Caudle.

Dr. Caudle:
Welcome to *Project Oncology* on ReachMD. I'm your host Dr. Jennifer Caudle, and joining me to discuss selective estrogen receptor degraders, or SERDs for short, and their role in treating advanced breast cancer is Dr. Nan Chen. Dr. Chen is an Assistant Professor of Medicine at the University of Chicago School of Medicine. Dr. Chen, welcome to the program.

Dr. Chen:
Thank you so much for having me.

Dr. Caudle:
Well, we're excited that you're here. So let's just dive right in. What are SERDs? And what role do they play in treating ER+/HER2- advanced breast cancer?

Dr. Chen:
Yeah, so SERDs are a novel class of drugs. We have been using an intramuscular SERD called fulvestrant for many, many years in the treatment of metastatic ER+/HER2- breast cancer. More recently, a new crop of drugs that are oral SERDs have been developed. These drugs are thought to maybe make it easier for patients to take these drugs; patients don't have to come in - they're pills - so they can take them at home. Additionally, we think that these drugs may be even more effective than fulvestrant themselves. And so there's been a lot of exciting research and a lot of exciting studies done in this area.

Dr. Caudle:
Excellent. And how do SERDs work to treat this type of advanced breast cancer?

Dr. Chen:
ER+ breast cancers are defined by the presence of estrogen receptor on the extracellular membrane. And essentially, estrogen and progesterone will bind to these receptors and cause downstream effects, ultimately leading to cell growth and cell division and proliferation of tumor. And so there are a lot of different drugs that seek to block the estrogen receptor or modulate it or alter it in such a way where this pathway is no longer active, and these cells will starve and die. And so SERDs, or selective estrogen receptor degraders, essentially degrade the estrogen receptor so that even if there's estrogen floating around in the patient's serum, there's no receptor for it to bind to.

Dr. Caudle:
Excellent. And now what about their efficacy and safety? Are there any trends clinicians should be aware of?

Dr. Chen:
As I mentioned, there's an intramuscular SERD that is currently approved: fulvestrant. In terms of its efficacy, I certainly think this is a drug that's used in either the first-line or second-line setting. And there are certain situations in which it may be better than aromatase inhibitors, especially if patients have been on it in the adjuvant setting or in the first-line metastatic setting.

I think that the most important side effects with fulvestrant still are related to what I would consider menopause symptoms. So hot

flashes, joint stiffness, and vaginal dryness. In addition to that, there are some GI symptoms. So maybe a little bit of taste changes, nausea, or a little bit of loss of appetite.

I think with these new oral SERD drugs that are coming - none of them have been approved yet, although some may be in the upcoming year - I think still many of the side effects are similar. I think one of the biggest differences between these oral SERDs compared to fulvestrant or some of the other endocrine therapies is an increased chance of us seeing some of the GI side effects. And so taste changes, loss of appetite, nausea, vomiting, and diarrhea are a little bit more common with these drugs compared to some of the endocrine therapies we've been using for a long time.

Dr. Caudle:
For those of you who are just tuning in, you're listening to *Project Oncology* on ReachMD. I'm your host Dr. Jennifer Caudle, and I'm speaking with Dr. Nan Chen about the clinical utility of SERDs for the treatment of ER+/HER2- advanced breast cancer.

So Dr. Chen, if we switch gears and take a look at some of the available data on SERDs, what can you tell us about the designs and findings from recent clinical trials?

Dr. Chen:
So thus far, there has been one positive phase 3 randomized trial looking at oral SERDs in comparison to either fulvestrant, the intramuscular SERD, or aromatase inhibitors. This was called the EMERALD trial, and it utilized the drug called elacestrant. Again, that was the investigational agent and the standard of care comparator arm was either fulvestrant or an aromatase inhibitor.

This study involved patients who have metastatic ER+/HER2- breast cancer who had previously progressed on at least a CDK4/6 inhibitor and at least some type of endocrine therapy. Patients were allowed to have had received zero or one lines of chemo. And many of these patients had disease in their organs, not just in their bones.

So when patients received this drug, it was shown that patients responded to this drug better and were able to stay on this drug for longer. Their disease was controlled for longer with elacestrant as compared to fulvestrant or an aromatase inhibitor in the entire population. But more specifically, this effect was actually more pronounced in the subpopulation with what's called an ESR1 mutation.

An ESR1 mutation is a mutation in the estrogen receptor itself. And this is a resistance mechanism to some of our existing endocrine therapies. About half of the patients in this trial had an ESR1 mutation. And this is something that commonly we see in the clinic as patients are treated with endocrine therapy over time.

And so this was a positive trial. The progression-free survival was improved with elacestrant compared to the standard of care arm.

Dr. Caudle:
Thank you for that. And with that being said, is there anything we need to keep in mind when evaluating these kinds of clinical trials?

Dr. Chen:
It's really important to know what type of patients were included in this and whether that is a patient that would apply to whoever is sitting in front of you. And so this was a study that enrolled patients that progressed on at least a CDK4/6 inhibitor. They could have received up to one line of chemotherapy, but traditionally, this was used in either maybe the second or third line of therapy for patients with metastatic ER+/HER2- breast cancer.

I think that this was a well-designed study. It was randomized, it included over 250 patients, and it was able to demonstrate benefit in the entire cohort, especially in the patients with an ESR1 mutation.

I certainly think that toxicities are really important to discuss when evaluating whether any treatment is appropriate for a patient. In this study, I think that rates of GI toxicities were a little bit higher in the elacestrant arm as compared to patients who are receiving either fulvestrant or endocrine therapy alone.

Dr. Caudle:
And before we close, Dr. Chen, do you have any final thoughts on SERDs or the management of ER+/HER2- advanced breast cancer that you'd like to share with our audience?

Dr. Chen:
Yeah, I think that this is an area that's really rapidly evolving in the previous year as well as with what I imagine will be some changes in the upcoming year with commercially available products. I think that oral SERDs are an exciting new class of drugs that we would love to be able to offer our patients. This was one positive study. There have been other drugs of the same drug class, other oral SERDs, that have not shown positive results. And so certainly, to ask ourselves why some drugs are working better than others is a question that remains to be answered.

I think that we need to utilize this data in the setting and in the context of other drugs that we are using, for example, PIK3CA inhibitors such as alpelisib, as well as the mTOR inhibitor everolimus. There are other drugs in the endocrine space that are being developed, such as estrogen receptor PROTACs. And so how all of these drugs will need to be utilized together to best provide safe, effective medications for patients with metastatic ER+/HER2- breast cancer, I think these are questions that will need to be teased out in the upcoming years.

Dr. Caudle:
Well with these final thoughts, this brings us to the end of our program today. I'd like to thank my guest, Dr. Nan Chen, for joining me to discuss SERDs and their impact on the treatment of ER+/HER2- advanced breast cancer. Dr. Chen, it was great having you on the program today.

Dr. Chen:
Thank you so much for having me.

Announcer:
This episode of *Project Oncology* was sponsored by Stemline, a Menarini Group Company. To access this and other episodes in this series, visit ReachMD.com/Project Oncology, where you can Be Part of the Knowledge. Thanks for listening!