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Poster Pearl: Elacestrant + Abemaciclib for ER+/HER2- Metastatic Breast Cancer

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. Charles Turck.

Dr. Charles Turck:
This is *Project Oncology* on ReachMD, and I'm Dr. Charles Turck. Joining me to discuss the poster she presented at the 2024 American Society of Clinical Oncology Annual Meeting that takes a look at the preliminary findings from the ELECTRA study is one of the authors, Dr. Erika Hamilton. Dr. Hamilton is a board-certified medical oncologist at SCRI Oncology Partners and the Director of Breast Cancer Research at the Sarah Cannon Research Institute in Nashville. Dr. Hamilton, welcome to the program.

Dr. Hamilton:
Thanks so much for having me. Happy to be here.

Dr. Turck:
So to start us off, would you walk us through the rationale behind the ELECTRA study as well as the study design?

Dr. Hamilton:
Yeah. The ELECTRA study looks at a combination of two drugs that are actually already FDA-approved for hormone receptor-positive breast cancer, but not together. And so we're combining elacestrant, which is an approved oral SERD, with abemaciclib, which is an approved CDK4/6 inhibitor. Obviously, there's a lot of preclinical rationale as well as knowledge from the first-line setting that combining endocrine therapies with CDK4/6 inhibitors can really be helpful, and we have emerging data that looks like even in the second-line after a CDK4/6 inhibitor, that continued CDK4/6 inhibitor blockade can be helpful.

One of the unique twists of the study is that we're also particularly looking at patients that have brain metastases. So once we get out of establishing what dosage of these two drugs we're going to use, we're looking at patients with brain mets, which, surprisingly to me, always ends up being a little bit more common than I think for ER-positive breast cancer.

Dr. Turck:
And would you tell us a little bit about the primary and secondary endpoints and how you evaluated them?

Dr. Hamilton:
Yeah, absolutely. So essentially, the phase 1b was to determine what dose of the two drugs we should be giving together, again, because it's being combined for the first time. So there were three cohorts: the first cohort was dose-reduced elacestrant with dose-reduced abemaciclib, the second was elacestrant at full dose and dose-reduced abemaciclib, and then as you can guess, the third cohort was whether we could do a full dose of both of the drugs elacestrant and abemaciclib.

The primary objective was the recommended phase 2 dose there. When we go on to phase 2, this is the area where brain mets are actually required. They're enrolling an additional 41 patients. The primary objective there is actual objective response rate. So how well is this combination at the ideal dose really working for patients that have ER-positive breast cancer and brain mets?

Dr. Turck:
So zeroing in on the results, what have you seen so far as far as the efficacy of combination therapy on tumor response is concerned?

Dr. Hamilton:

Yeah, I'd love to share the results with you. I think before we do that, probably just telling you what these patients actually looked like in terms of prior therapies is important to put it into context.

Three quarters of the patients did have visceral metastatic disease. Most patients had seen fulvestrant, so the intermuscular version of a SERD. Almost all had seen CDK4/6 inhibitors. And about 1/2 had already seen chemotherapy. So a pretty consistent population in terms of a phase 1 study and a little bit more heavily pre-treated.

What we determined was that the full dose of both drugs was tolerated. And this is fantastic—so giving elacestrant and abemaciclib at full dose—and we saw one complete response and four partial responses out of the first 26 patients enrolled. So this actually translated to a clinical benefit rate of 73 percent because we saw quite a few patients that had stable disease but control of their disease without progression, and we did not see any drug-to-drug interactions between the two drugs as well.

Dr. Turck:
For those just tuning in, you're listening to *Project Oncology* on ReachMD. I'm Dr. Charles Turck, and I'm speaking with Dr. Erika Hamilton about preliminary data from ELECTRA, which is an open-label, multicenter phase 1b and 2 study.

Now looking further at the study's findings, Dr. Hamilton, you mentioned a little bit about tolerability. What else can you tell us about safety?

Dr. Hamilton:
Yeah, absolutely. I think this is a really important question because when we combine drugs, we tend to add side effects. And so it's always tempting, particularly in our endocrine therapies, to do combinations, but we really need to make sure that they're still quite tolerated for our patients.

Some of our other drugs in this space, the PI3 kinase inhibitors, maybe even mTOR or Akt, can be a little bit of a struggle in terms of tolerability. We know that abemaciclib can cause diarrhea. I think we've gotten better at managing that, but it's a very prominent side effect. So what we saw that was the most common grade 3 or greater adverse event was actually neutropenia. This makes sense because we're using a CDK4/6 inhibitor, and it happened in about 1/4 of patients.

Other than that, there were almost no grade 3 or grade 4 adverse events in the study, which was really reassuring. And in fact, no diarrhea was greater than grade 1 or grade 2, so really successfully giving this oral SERD with abemaciclib without worsened diarrhea. About 50 percent of patients have had some grade of diarrhea, but again, all grade 1/grade 2, no more severe cases of diarrhea. And again, full dose of both drugs were tolerated together without any grade 4 treatment-emergent adverse events. So I think pretty reassuring news.

Dr. Turck:
And you had mentioned a lack of drug/drug interactions. Is there anything else that you can tell us about the pharmacokinetic profiles of elacestrant and abemaciclib?

Dr. Hamilton:
No, I really think the concern was about any potential drug/drug interactions that was going to change the intended dose of one of these, but we did not see this, and luckily, even with combining them, it looks quite safe.

Dr. Turck:
Well, thank you for sharing all those findings with us, Dr. Hamilton. Now before we close, would you tell us what's next for the ELECTRA study?

Dr. Hamilton:
Yeah. I think that this is quite exciting. We're still enrolling patients into the brain mets-required cohort to see about our activity. Abemaciclib as a single agent wasn't quite as promising in terms of brain mets as we'd hoped it was, but elacestrant with abemaciclib, we really have quite high hopes for. I think that this combination of endocrine therapy is really exciting, with more evidence that CDK beyond CDK looks like it helps our patients. And it looks like most patients in the first-line setting are getting ribociclib or palbociclib. So abemaciclib seems well-poised to be a combination here in the second-line setting.

Dr. Turck:
Well, with those forward-looking thoughts in mind, I want to thank my guest, Dr. Erika Hamilton, for joining me to discuss the preliminary findings from the ELECTRA study. Dr. Hamilton, it was great having you on the program.

Dr. Hamilton:
Thanks so much for having me.

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