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Selecting Therapy for ER+/HER2- Metastatic Breast Cancer: Key Factors to Consider

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. Turck:
Welcome to *Project Oncology* on ReachMD. I'm Dr. Charles Turck, and joining me to discuss the various factors that guide treatment decisions for patients with ER+/HER2- metastatic breast cancer is Dr. Megan Kruse, who's a breast medical oncologist at Cleveland Clinic in Ohio. Dr. Kruse, welcome to the program.

Dr. Kruse:
Hi, thanks for having me.

Dr. Turck:
So to start us off, Dr. Kruse, what are the key disease-related factors you consider when selecting a treatment option for a patient with ER+/HER2- metastatic breast cancer?

Dr. Kruse:
So when it comes to disease-related factors for patients in this situation, I think the most important thing to keep in mind is if the cancer has been treated previously – meaning in the early stage setting – and what the response to that treatment was. We certainly take a different approach to treatment based on if a patient had recurrence of their cancer or metastatic spread of their cancer while on anti-estrogen therapy or if this is a brand new diagnosis for them. And then if the cancer has returned after a prior endocrine therapy, we take into account how long the patient has been off of the endocrine therapy in terms of making the next treatment selection. The other disease-related factors that are really, really important is the sites of involvement of the cancer and the amount of symptoms that those sites of involvement are causing for our patients. Historically, if a cancer has involved a lot of organ-based or visceral sites and if there was a threat to organ function from the cancer, this would be a situation in which we would reach for combination chemotherapy. But we know from more recent studies that have been presented that anti-estrogen-based therapy actually has a very meaningful role in controlling cancer for these patients. It actually tends to work better – meaning longer term control – and also works in about the same amount of time that combination chemotherapy does. So while I would say that the degree of visceral involvement of the cancer has historically been a big differentiating point in this space, I think it's still important to know, as these patients will have to be supported through, but it may not have as much of an impact on our treatment decision compared to those patients who do not have a high organ involvement burden at diagnosis.

Dr. Turck:
And how do patient-specific factors, things like patient fitness and access to therapy, how do you take those into account when determining a treatment course?

Dr. Kruse:
I actually think the patient level factors are probably the biggest portion of what we consider when we're making treatment decisions for patients with hormone receptor positive metastatic breast cancer. And this has a lot to do with the fact that there are many options, and the patients may feel differently about the options based on the logistics of treatment and the impact that that may have on their quality of life, like how often they have to be at a treatment center or in a doctor's office. The individual side effects that might go along with each of the treatments I think has a lot to do with patient preference, but also many times the other medical problems that they come to their cancer diagnosis with and those may actually be exacerbated by some of our treatments. And at the end of the day, the goal is to keep the patients living longer and living better, so if we're doing something with our cancer treatment to make their other medical problems worse, we may not necessarily be fulfilling that goal. And I think that there's another big burden to talk about here, which is

actually the financial impact of all of this. Thankfully, many of our treatments in this setting are oral or pills, and that allows some convenience on the patient standpoint, but it also means that we're thinking about outpatient payments, copays, and the actual accessibility to the drugs themselves. And so that can be a huge factor when we're walking through the initial treatment discussions with patients.

Dr. Turck:
You talked a little bit about patients' own priorities and goals. How do you determine what matters most to them when it comes to selecting a treatment approach?

Dr. Kruse:
Yeah, I think the way to approach patient preference really just involves some good, careful conversation, and so for me, this looks a little bit different depending on if I'm meeting a patient for the first time or if this is a patient that I've had an ongoing relationship with. You know, for those of our patients that we treat in the early-stage setting and unfortunately have recurrences, many times we have a relationship with that patient where we've talked about what's important to them. We may know the activities of life that they enjoy, what their family situation is like, what some of the barriers to treatment might be, and so we might start with a leg up on that. For patients we're meeting for the first time, I think it's important to explore all those same features of their lives, although that can be a tough conversation when we know we have a lot of medical ground to cover. So sometimes this conversation really has to happen in a staged way, where we deliver a lot of information, but also hear back from patients. And sometimes, they actually need a little bit of time to think about it before arriving to the best decision that's right for them.

Dr. Turck:
For those just joining us, this is *Project Oncology* on ReachMD. I'm Dr. Charles Turck, and here with me today is Dr. Megan Kruse, who's talking about treatment selection considerations for patients with ER+/HER2- metastatic breast cancer.

So, Dr. Kruse, switching gears a bit and taking the focus back to the therapeutic landscape, what are the treatment options available for patients with ER+/HER2- advanced disease?

Dr. Kruse:
For these patients, there are many different treatment options, and they fall into categories that are largely antihormone or endocrine-based therapies and then chemo-based therapies. I would say for the vast majority of patients in this setting, we start with some sort of endocrine-based option, and that's usually the combination of either an aromatase inhibitor or a SERD – a selective estrogen receptor degrader or down-regulator – in combination with a CDK4/6 inhibitor. So in the first-line treatment for these patients, the greatest benefit has been associated with the combination of endocrine therapy and a CDK4/6 inhibitor. And thankfully, with that type of treatment, most patients are able to have over a year – often two years or more – of cancer control with the same stable therapy. And usually, those therapies are quite well tolerated, convenient, and fit into a patient's life pretty well. And then beyond that, we start to think about other maybe targeted treatment options based on different biomarkers that might be present in a patient's cancer, and then ultimately when the cancer develops some endocrine resistance, we start moving on to more chemotherapy-based options, of which there are multiple.

Dr. Turck:
And as a quick follow-up to that, would you highlight some key data supporting the use of those options that might influence your treatment selection?

Dr. Kruse:
Absolutely. So in the last year or so, we've had a number of studies in this space that have really impacted the overall survival results for patients with hormone receptor positive metastatic breast cancer. Some of the key pieces of data that we have here are those from the DESTINY-Breast04 study, the EMERALD study, and the TROPiCS-02 study.

And so starting with DESTINY-Breast04, this was a study that actually opened up the treatment landscape of HER2-low disease for patients with hormone receptor positive metastatic breast cancer. So diving into that a little deeper, what that means is for patients that were traditionally considered HER2-, and that includes those with HER2 immunohistochemistry results of 1+ or 2+ and in situ hybridization testing which is negative, these patients were actually treated with one of our newer antibody drug conjugates – trastuzumab deruxtecan – versus our traditional, single agent chemotherapy. And what we found was for those patients that now qualify as HER2-low, there was actually a progression-free survival and overall survival benefit associated with the use of trastuzumab deruxtecan. So this is actually a big, big step forward, not only because it improves overall survival, but also because it's opening up kind of a fourth disease state within metastatic breast cancer – the HER2-low space – in addition to what we traditionally think of.

Dr. Turck:
Now you also mentioned the EMERALD and TROPiCS-02 studies. So would you walk us through some of those data as well?

Dr. Kruse:
The other studies that I referenced led to new drug approvals here in 2023. So for the EMERALD study, this was the study that ultimately led to the FDA approval of a new oral SERD elacestrant for patients with ESR1 mutations as part of their hormone receptor

positive, HER2- metastatic breast cancer. And in this study, the elacestrant was compared to other standard endocrine therapy options for patients who had received one prior endocrine therapy for their hormone receptor positive metastatic breast cancer. The progression-free survival benefit was really encouraging, particularly for those patients with the ESR1 mutations who remained endocrine sensitive and actually those who had longer duration of prior CDK4/6 inhibitor. They actually had better benefit in terms of PFS for the elacestrant. So this is another great option that has been opened for our patients. It's oral, it's more convenient, it's another endocrine-based therapy, so these are all things that patients are very interested in after their first-line CDK4/6 inhibitor-based therapy, many of which do very, very well on for a long period of time.

And then the last study that I wanted to comment on was on the TROPiCS-02 study. And this study actually looked at a drug that we're familiar with in a different disease state. So this is looking at sacituzumab govitecan, which has been approved for metastatic triple negative breast cancer and now approved for metastatic hormone receptor positive, HER2-negative breast cancer based on the TROPiCS-02 study, as I mentioned, that showed improvement in progression-free survival and overall survival. And this is a really interesting study because it actually took patients that were more heavily pretreated, who had received multiple prior lines of chemotherapy, and yet we still saw benefits in both progression-free survival and overall survival, which is a high bar to meet in this heavily pretreated population. And because this is a drug that we're familiar with, while it has toxicities such as gastrointestinal toxicity in terms of nausea, diarrhea, and also neutropenia, these are things that we as oncologists are familiar with tackling. And so it really, again, expands our treatment arsenal for patients in this hormone receptor positive metastatic space.

Dr. Turck:
And lastly, Dr. Kruse, are there any key takeaways you'd like to leave with our audience today?

Dr. Kruse:
Yes, so I think my biggest takeaway as we approach treatment in this space is really the importance of biomarkers. So for the longest time, breast cancer has been a biomarker-driven disease. We lump our patients' diagnoses into these categories of hormone receptor positive or negative, HER2+/-, and now HER2 low, but our biomarkers that we need to be aware of just keep expanding. So being able to get biomarker testing along the way – whether that's from tumor tissue itself or from circulating tumor DNA in the blood – I think these are really important conversations to be having with our patients and crucial to knowing what the best treatment options are for them. And then getting this information over time is really important because there are some mutations that we will see over the lifespan of the cancer, for example, a BRCA mutation or a PIK3CA mutation tend to be early events in the cancer's lifetime. But then other mutations like ESR1 are mutations that are acquired and come with resistance to prior treatment, and so I think knowing the pattern of when these biomarkers emerge, when we expect to see them, and how that influences when we get biomarker testing is crucial as we move forward in this space.

Dr. Turck:
Well as those final thoughts bring us to the end of today's program, I want to thank my guest, Dr. Megan Kruse, for joining me to share guidance around selecting treatment options for patients with ER-positive, HER2-negative metastatic breast cancer. Dr. Kruse, it was great having you on the program.

Dr. Kruse:
Thanks so much. It was great talking with you today.

Announcer:
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