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Addressing Unmet Needs in HER2-Low Breast Cancer Care

Announcer:
You're listening to *Project Oncology* on ReachMD. This episode is sponsored by Daiichi-Sankyo. Here's your host, Dr. Charles Turck.

Dr. Turck:
Welcome to *Project Oncology* on ReachMD. I'm Dr. Charles Turck. And here with me today to explore the unmet needs of our patients with HER2-low breast cancer is Dr. Maryam Lustberg, Associate Professor of Medicine in Medical Oncology at Yale School of Medicine. She is also the Director of the Breast Center at Smilow Cancer Hospital and Chief of Breast Medical Oncology at Yale Cancer Center. Dr. Lustberg, welcome to the program.

Dr. Lustberg:
Thank you so much. Very glad to be here today.

Dr. Turck:
To start us off, Dr. Lustberg, would you give us an overview of the current treatment landscape for HER2-low breast cancer?

Dr. Lustberg:
Yes, of course. So this is an area that's rapidly changing, which is very exciting for our patients. We traditionally did not think of breast cancer subtypes as HER2-low. They were either negative or positive. And so a tumor would either be in that estrogen receptor positive, HER2 negative type subtype being luminal A or luminal B, or being more in that basal subtype or a triple negative with the HER2 status negative. If they met criteria for HER2 positivity through immunohistochemistry or fluorescent in situ hybridization, they would be classified as HER2 positive. So until very recently, the idea that tumors could be HER2-low actually didn't exist, and I think this is an area that will be rapidly changing in the coming years.

Dr. Turck:
And what are some of the most common challenges and limitations associated with treatment options?

Dr. Lustberg:
So when we think about traditional HER2-low tumors falling into those two broad categories that I mentioned of endocrine positive tumors or triple negative tumors, essentially what has been available after targeted therapies and immunotherapies has been the older traditional chemotherapies, which have had limited success. So I would say that has been one of our biggest challenges is that by the time that endocrine positive tumors need chemotherapy, we go through several lines of chemotherapy. And after the second or third line, there's really a limited treatment response that we unfortunately see in many patients. And similarly in triple negative breast cancer, even if we're starting with a newer immunotherapy combinations, once they unfortunately progress, essentially the barrier that we face is that the responses tend to go down after several lines of chemotherapy.

So we absolutely need new or better strategies. And thinking of the HER2-low tumors as an entity that could be more targeted specifically, I think is a very important strategy that we're beginning to study in clinical trials.

Dr. Turck:
So with those obstacles in mind, would you tell us about some of the attendant unmet needs for patients with HER2-low breast cancer?

Dr. Lustberg:
I would say I would categorize these challenges as two primary challenges. One is that we essentially have not had a formal way of addressing what HER2-low really means, whether it can be actually targeted with specific HER2 directive therapies. So as a

consequence, they've had less therapies being available to them. And this is something that we are working on changing through dedicated clinical trials.

The second challenge has been even how do we characterize a tumor as HER2-low versus HER2 positive versus HER2 negative? It seems that we have more and more data that some of our traditional ways of ascertaining HER2 status may not always give us the most precise answer in terms of which tumors are actually being driven by HER2-related pathways. So even how we characterize a tumor as HER2-low, if you take two different pathologists, they may come up with very different answers as to who is HER2-low versus not. So improving our diagnostics and our biomarkers in terms of how we categorize our breast tumors, this is an exciting area that's rapidly improving, and I expect a lot of advances in the coming years.

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. Maryam Lustberg about the treatment limitations associated with HER2-low breast cancer and the resulting unmet needs of patients.

So, Dr. Lustberg, now that we've discussed the unmet needs of our patients with HER2-low breast cancer, how might developments in the therapeutic landscape help address them?

Dr. Lustberg:
So there are lots of wonderful opportunities and questions being asked in the context of clinical trials, none are quite ready for prime time. However, we're getting close. And these are in the realm of a new set of drugs known as antibody drug conjugates. And this is a smarter way of delivering chemotherapy where the payload, the actual chemotherapy, is actually directly entering the areas that have a specific marker. And this class of drugs, there is not just one; there's a whole slew of antibody drug conjugates and many of them are specifically focused on HER2 pathways. These drugs are showing a lot of promise for both HER2 positive tumors, the traditionally classified HER2 positive tumors, but also we're beginning to see some encouraging data that the HER2-low tumors may also very much respond to these HER2-directed antibody drug conjugates. So I would say this is the most exciting area of development still in clinical trials, although we hope to have some more definitive answers in the near future.

Dr. Turck:
And if we look beyond the treatment landscape for just a moment, Dr. Lustberg, what are some of the other ways we can work to address our patients' unmet needs?

Dr. Lustberg:
So I think in addition to innovative therapeutics, what goes hand in hand with that is personalizing how we manage symptoms and toxicities and really deliver patient-centered care. The more we're able to complement these two areas and really see that dedicated symptom management personalized to each patient is really just as important as picking the right drug for them. And that by optimizing symptoms we can actually deliver our more exciting therapeutics in a safer, more effective and efficacious way. I think this is an area that is also improving. We still have a ways to go, but it is a passion of mine as well as many others. And patients and families have spoken loud and clear that quality of life and supportive care are equally important to them as drug therapies. So really what I envision is that these two areas will become much more complementary and integrated in the coming years.

Dr. Turck:
Before we close, do you have any other thoughts you'd like to share with our audience today?

Dr. Lustberg:
I want to express a lot of hope for the future. I believe the future of breast cancer therapeutics is looking very bright with a lot of exciting therapeutics, including in the area of antibody drug conjugate therapy that I mentioned earlier. And then also a lot of exciting work in the realm of innovative biomarkers, so we can better select patients for the right therapies. And in addition to these, continuing to personalize that symptom management trajectory, and making sure that we're paying as much attention to therapeutics as to quality of life issues. I think we're making good progress on that. And I expect a lot of innovation in the coming years in all of these areas.

Dr. Turck:
Well with those final thoughts in mind, I want to thank my guest, Dr. Maryam Lustberg, for sharing her perspective on how we can better address the unmet needs of our patients with HER2-low breast cancer. Dr. Lustberg, it was great speaking with you today.

Dr. Lustberg:
Thank you so much. Thank you for these wonderful questions.

Announcer:
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