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Selection and Sequencing of ADCs in HR+/HER2-Low MBC

Announcer:
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Dr. Mayer:
Hello, I'm Erica Mayer from Dana Farber Cancer Institute. And I'm joined today by my wonderful colleague, Dr. Sarah Sammons. And we're here to talk about antibody drug conjugates for HER2-low breast cancer. So welcome.

And, you know, it's I'm just so excited that we now have, right now, two, and possibly in the future, more antibody drug conjugates, which have entered our treatment space for HER2-low hormone receptor-positive disease. It's been a wonderful thing for us and for our patients. But sometimes it feels like we are benefiting from too many riches when we're trying to figure out how best to deploy these agents in clinic. And, Sarah, I wanted to talk to you a bit about, how do you make decisions about which agent to use? We have T-DXd, and we have sacituzumab govitecan, both of them excellent agents for this disease space. If we have a patient who's coming in with, let's say, endocrine-resistant disease, who's moving into the chemotherapy space, how do you think about for that patient which drug to use, when?

Dr. Sammons:
Yeah, it's a really good question. And, you know, for the longest time after endocrine resistance, all we had was chemotherapy. And chemotherapy does not work particularly well. So to have these new agents is fantastic.

The first thing that I think about is what is the HER2 status? So the previous paradigm was HER2-positive or HER2-negative, and that's the case no longer since HER2-low is now a biomarker for efficacy for trastuzumab deruxtecan. So I'm looking at their most recent biopsy to see if they're HER2, if they are HER2-low. If they're not on their most recent biopsy, I'm looking at all of the prior biopsies because if they've ever been HER2-low at any point of time, then I would consider trastuzumab deruxtecan for those patients. And, you know, right now, unless the patient has a contraindication to receiving it from a toxicity standpoint, for HER2-low patient trastuzumab deruxtecan is the first ADC that I would use after at least 1 line of chemotherapy. And I'm wondering if you feel the same way? How are you doing that?

Dr. Mayer:
Yeah. So I think that's a great point about searching all the pathology. I put a patient on T-DXd the other day with my HER2-low results from 2010. So you can't go back too far, you just have to find something. And, you know, I think we all found the data from DESTINY-Breast04 so compelling, showing in patients who have had at least 1 prior line of chemotherapy that using T-DXd provided superior progression-free and overall survival results, compared to a treatment of provider choice, which had some really good choices that we, you know, otherwise would routinely be using in clinic. So I definitely agree with you that, you know, unless there's a major toxicity contraindication or patient preference issue that that does, you know, based on the data, that does tend to be a preferred option.

But what if the patient is truly HER2-0? Like you cannot find HER2 anywhere in their pathology?

Dr. Sammons:
Yeah, sure. And it happens, it does happen, I would say it's about maybe one-third of our hormone receptor positive patients are truly HER2-0. And for those patients, certainly my first ADC of choice and 2023 will be sacituzumab govitecan. And currently, the FDA approval is after 2 lines of chemotherapy. And I know that it's being looked at in earlier lines, which we're all excited about, but certainly in our HER2-0 populations, sacituzumab would be the first ADC that I would use.

Dr. Mayer:
And you know, I think the big question is, you know, we've seen beautiful responses on T-DXd, but eventually things can worsen. And when we are getting into the third-line space, you know, considering the TROPiCS-02 data, we do have available sacituzumab. What are your thoughts on sequencing ADC after ADC? Do we have any data for that? Or how are you approaching that?

Dr. Sammons:
So really good question. It's a data-free zone but there are many clinical trials going on looking at ADC after ADC. You know, does a different target matter when it's a similar payload which is sacituzumab and T-DXd. You know, right now, I still would give sacituzumab a try after trastuzumab deruxtecan or T-DXd. And there are ongoing trials looking at the efficacy. I think we're all a little bit worried that the efficacy will be a little bit less. But since we're comparing it to options that are not so great, just, you know, run-of-the-mill chemotherapy, I still think it's worth a shot.

Dr. Mayer:
I agree. And of course, as you just said, putting someone on a trial would probably be our preferred approach in that setting so we can learn from the experience.

So I want to thank everyone for listening. I hope this was a helpful conversation.

Announcer:
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