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How Genetic Testing Guides Personalized mBC Care

Announcer:
This is *On the Frontlines of Metastatic Breast Cancer* on ReachMD. Here's your host, Dr. Alexandria May.

Dr. May:
You're listening to *On the Frontlines of Metastatic Breast Cancer* on ReachMD, and I'm Dr. Alexandria May. Today I'm joined by Dr. Marie Wood, Professor of Medical Oncology at the University of Colorado Anschutz School of Medicine, to discuss genetic testing in breast cancer. Dr. Wood, thanks so much for being here today.

Dr. Wood:
Thank you so much for having me. It's a pleasure.

Dr. May:
Let's start with some context, Dr. Wood. How has the role of genetic testing in breast cancer evolved in recent years?

Dr. Wood:
I think the role of genetic testing has really expanded. We've refined our eligibility for genetic testing, but I also think it's really important to realize that we now make treatment decisions based on genetic testing. For example, we now have PARP inhibitors for people who have BRCA1, BRCA2, or PALB2 mutations. We also know that if people have deficiencies that are associated with microsatellite instability, which can be associated with other genetic syndromes such as Lynch syndrome, that may change their eligibility for specific treatments.

We know that the guidelines suggest that we test the majority of patients at diagnosis. It's always important to remember to test somebody when they've developed metastatic disease. I think sometimes people get overwhelmed with all the things that need to happen for a newly identified patient with metastatic disease, but it's important to realize that genetic testing has treatment implications.

Dr. May:
I'd like to dig into that a little deeper. What distinctions are important for clinicians to understand between germline and somatic testing in breast cancer?

Dr. Wood:
That's actually a great question, and sometimes I think people confuse the two because it's all DNA-based. Somatic testing often tells you about the changes in the tumor. It can also reveal germline mutations—being things that you're born with—but you have to know how to tease those two out of the report. When we're looking for germline variants such as BRCA1 or BRCA2, we can do a blood test or a saliva test. When we're looking for somatic-based tests, we test the actual tumor. Sometimes, we're also testing circulating DNA. We can tell a patient has a germline variant by looking at the allele frequency of the mutation in that tissue. When it's very high, it can signify that that mutation is potentially a germline mutation. The only way to tell is by doing subsequent germline testing.

Dr. May:
And with that being said, what factors do you consider when determining whether a patient may benefit from genetic testing?

Dr. Wood:
So the first question in the metastatic setting I ask is, will it change management? I just told you we now have PARP inhibitors. We also know that certain germline mutations are associated with certain chemotherapy sensitivity, with BRCA1 and BRCA2 being more sensitive to PARP inhibitors. At other times, and I told you a little bit about immunotherapy, we do PD-L1 testing, but identifying

microsatellite instability associated with Lynch syndrome can identify a patient for whom you change their treatment plan.

The other thing that I think is important to remember is that testing a patient with cancer and remembering to do that avoids a missed opportunity. So many patients come to genetic counseling without cancer and have a family history, but that patient with cancer—whether it's at their diagnosis and the tumor is removed or whether it's metastatic disease—they're the best candidate for genetic testing.

Dr. May:
For those just tuning in, you're listening to *On the Frontlines of Metastatic Breast Cancer* on ReachMD. I'm Dr. Alexandria May, and I'm speaking with Dr. Marie Wood about the role of genetic testing in contemporary breast cancer care.

So, Dr. Wood, moving on to treatment now, how are genetic testing results influencing breast cancer management decisions?

Dr. Wood:
I think there are two things to consider to answer that question. One is the metastatic setting, and one is the newly diagnosed and either neoadjuvant or adjuvant. We know that genetic testing can influence upfront treatment, such as what surgery you do. Is the patient somebody who would like a bilateral mastectomy at their diagnosis? It can also influence adjuvant therapy. We know that PARP inhibitors are very effective in reducing the risk of recurrence and improving overall survival for patients with BRCA1 or BRCA2 tumors, regardless of whether they have triple-negative cancer or ER-positive cancer.

The metastatic setting, as I've alluded to, can offer treatment options. Whether we use a PARP inhibitor in the frontline setting may depend upon the rest of the prognostic profile of the cancer and the disease burden. But we have good evidence that patients can respond if they have BRCA1 or 2 or PALB2 mutations. We also have a new study to offer our patients who have metastatic disease with germline BRCA1, BRCA2, or PALB2 mutations and are ER positive that's asking the question: is combining a PARP inhibitor with endocrine therapy a good way to go in the frontline setting? We tend to use one or another. So I think that's an important study; it's called the EvoPAR study.

Dr. May:
And as a follow-up to that, what role does genetic counseling and family communication play in the broader testing process?

Dr. Wood:
That's another great question. I think that we used to want to make sure that every patient had genetic counseling and understood the pros and cons, risks and benefits, and potential results of genetic testing upfront, including things like insurance implications. But I think there are other ways that we can do genetic counseling upfront. We now have videos that can explain genetic testing, papers, and there are even studies looking at chatbots.

It's not to say that genetic counseling isn't important, but trying to get a person into a queue to get an appointment with a genetic counselor when they have metastatic disease is a big barrier to getting that testing done. And hopefully, what you've heard from me is that testing is so important, not only for themselves and their cancer treatment, but for their family members. I think it's really important that anybody who has a positive mutation does ultimately see a genetic counselor because they really need to understand what that mutation means for them and for their family.

I also think that patients who have what's called a variant of uncertain significance identified on genetic testing really need to have genetic counseling. Those patients sometimes are confused, as are their providers, that this is a test that we can act on, and that is not the case. The other place where seeing a genetic counselor can be helpful is if a patient tests negative but has a positive family history, what does that mean? What should we recommend for the patient and for their family?

The other part that's really important is this concept of cascade testing, which does require family communication. We know from other studies in other syndromes, such as Lynch syndrome, that we are very bad at doing cascade testing, whether the patient sees a genetic counselor or whether they're a patient that we've just tested in our clinic. So we need new models to do that, but meeting with a genetic counselor and understanding the importance of family communication is one of the first steps to move forward with cascade testing.

Dr. May:
Before we wrap up, Dr. Wood, do you have any final thoughts you'd like to share with our audience?

Dr. Wood:
I think what I'd like to let our audience know is the importance of testing a patient with metastatic cancer. Many patients today get testing at their diagnosis because it matters for their surgery or potentially their adjuvant therapy. But sometimes, patients who come back with metastatic disease haven't had genetic testing, or patients with de novo metastatic breast cancer haven't had genetic testing.

It's so important to make sure that all patients with breast cancer who are candidates for testing have testing. It's important for their

treatment. It's also important, as I've mentioned, for their family.

Dr. May:
With those important takeaways in mind, I want to thank my guest, Dr. Marie Wood, for joining me to discuss how genetic testing fits into breast cancer management. Dr. Wood, it was great having you on the program.

Dr. Wood:
It was a pleasure being here. Thank you for inviting me.

Announcer:
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