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Combatting Breast Cancer with Chemoprevention

Dr. Sands:
Breast cancer is the most common cancer in the US and the second most common cause of cancer mortality among women in the US. But can chemoprevention help reduce the rates of this fatal disease?

Welcome to *Project Oncology* on ReachMD. I'm Dr. Jacob Sands. And joining me today to talk about breast cancer prevention is Dr. Marie Wood, the Director for Breast Medical Oncology and Director of the Cancer Clinical Trials Office at the University of Colorado Anschutz Medical Center.

Dr. Wood, thank you for being here today.

Dr. Wood:
Thank you. It's a pleasure.

Dr. Sands:
So let's dive right in. When evaluating a patient with breast cancer, what factors do you take into consideration to determine whether they're a candidate for breast cancer chemoprevention?

Dr. Wood:
So I think there are three types of risk factors that put women in a situation where they could consider chemoprevention. One is a family history. If you have a family history that suggests that you're at moderate or high risk, you could consider chemoprevention. Additionally, women who carry certain predisposition mutations, not always the most common but certainly BRCA2 mutation carriers, sometimes ATM or CHEK2, those mutations that put you at risk for ER-positive breast cancer; and then women who have biopsies showing some atypia, such as atypical ductal hyperplasia, atypical lobular hyperplasia or just atypia, those women have a significant risk in the range of 20 to 30 percent over their lifetime and are probably the best candidates for chemoprevention.

Dr. Sands:
Now, what are some of the currently available treatment options for chemoprevention?

Dr. Wood:
So we have several options at this time. For premenopausal women, the only option is tamoxifen. And the exciting thing about tamoxifen is that there is a new study that shows that a lower dose may be just as effective as a higher dose. There are three aromatase inhibitors, and any one of them could be used but only for postmenopausal women. There is some data showing that raloxifene can reduce the risk, but I think raloxifene is really best for women who have low bone density and are looking to improve that.

Dr. Sands:
And as a follow-up to that, would you say that these are agents being used in clinical practice? And if so, how widely?

Dr. Wood:
So I would say, Dr. Sands, that they are not being used, and there are a lot of barriers to use. Tamoxifen and the aromatase inhibitors do have a side effect profile, and if you don't have cancer, you're going to be less likely to tolerate that side effect profile as opposed to if you do have cancer and you're thinking about preventing a recurrence and improving your overall survival, so toxicity is really, really important. For tamoxifen we have concerning side effects, such as blood clots and uterine cancer and cataracts. The side effects of hot flashes and sexual dysfunction are huge barriers. For the aromatase inhibitor, we have lowering bone density as a concerning side effect as well as arthralgias and hot flashes. Interestingly, the low-dose tamoxifen study did show that there were very few side effects

with a dose of five mg daily. In the US, that dose would have to be 10 mg every other day, but that seems to be much more tolerable, so I think that we can consider that.

The other barrier to use is physician recommendation. I don't know that all these women with these risk factors are always seen in a place where we could consider those, but we know that physician or provider recommendation is a key barrier to use of these endocrine options for chemoprevention. Additionally, these options only prevent ER-positive breast cancer, so for women who have higher risk of ER-negative breast cancer, such as BRCA1 mutation carriers or African-American women, these may not be the best options.

Dr. Sands:
For those just tuning in, you're listening to *Project Oncology* on ReachMD. I'm Dr. Jacob Sands, and I'm speaking with Dr. Marie Wood about considerations for breast cancer chemoprevention.

Now, Dr. Wood, you've outlined, some the challenges, I suppose, in treating, sounds like estrogen receptor-positive disease. Are there any other, limitations to outline, regarding that or any other subtypes of breast cancer to further discuss?

Dr. Wood:
Well, I think it's important to just highlight the prevention of ER-positive breast cancer. So, when you look at the overall incidence of breast cancer, the majority of breast cancers are ER-positive. I think it's difficult if you have a lesion, such as benign breast disease, or a family history to know whether you're at risk for ER-positive or ER-negative breast cancer. I think that these agents really are useful. They do prevent only ER-positive breast cancer. So, when you look at the clinical trial data, you see that there was a significant—greater than 30–50 percent—reduction in the development of breast cancer. For those women who had benign breast disease, in one trial that risk reduction was almost 80 percent, but it does only reduce ER-positive breast cancer. To date, we don't have agents which can reduce the risk of ER-negative breast cancer.

There have been a lot of clinical trials looking at drugs like metformin, looking at statins, looking at vitamin D, looking at aspirin. To date, none of them have shown the effectiveness that we want in moving them forward in a large clinical trial. There is a specific clinical trial for women with BRCA1 mutation carriers suggesting that denosumab may be able to prevent breast cancer in that population, so that's a really interesting study. And there are additional clinical trials looking at things like diet and exercise and things like that that may be beneficial.

Dr. Sands:
Now, you've outlined some of the, really significant potential risks, uh, as well as reasons for, people essentially choosing not to be treated, or it sounds like even related to the counseling itself. Are you able to kind of piece these together for us now as to how you'd recommended or what the guidelines are as far as moving forward with these treatments and essentially handling some of these, these potential risks?

Dr. Wood:
That's a great question. I think that the guidelines certainly suggest that women at above average risk should be offered these agents. That said, in my opinion, the place to consider it is women who have a strong family history and thinking about those women who have multiple first-degree relatives with breast cancer would suggest a strong family history. I think every woman who has a biopsy showing benign breast disease—and as I said, that's an atypia on the biopsy specimen, whether it's atypical hyperplasia or ductal hyperplasia or lobular hyperplasia—is probably the most significant category where these agents can be helpful. I think also certain mutation carriers, those that we know have a higher risk of ER-positive breast cancer, such as BRCA2, CHEK2, ATM, and there are others, so trying to talk to your primary care provider or breast health specialist. There are many centers across the country focused on breast health, and it's common that there are individuals, such as APPs, nurse practitioners or physician assistants, who have expertise in this area and can consult with women to talk about the risk and benefit of these agents and if it's right for them.

It's important to remember that the only agent we have for the prevention of breast cancer for premenopausal women is tamoxifen, and for post-menopausal women, that is the aromatase inhibitors. And for anybody contemplating this worried about the toxicity profile, I think low-dose tamoxifen is really an important, new option that we have for women at risk.

Dr. Sands:
And if we look to the future, are there any treatment agents on the horizon for chemoprevention?

Dr. Wood:
So I mentioned denosumab for women with BRCA1 mutations. There are clinical trials that are looking at other options, such as topical agents. There are a couple clinical trials looking at tamoxifen-like compounds that can be applied directly to the breast and, have shown good effect in the reduction of the risk of breast cancer. We hope that there will be other trials of novel agents or novel combinations of agents, and this is one of the things that I'm particularly interested in, such as compounds like vitamin D or metformin or aspirin or

statins or even a combination of those, but I don't believe that there are any clinical trials available.

Dr. Sands:
And before we close, Dr. Wood, I'd like to give you the final word. Are there any thoughts or takeaways that you'd like to leave the audience with today?

Dr. Wood:
I think the most important thing is to think of prevention. It's something that's a little bit hard to think about. I think primary care providers have a lot on their plate, and trying to think about offering chemoprevention to women is not always on their plate, but I think thinking about it is key, and I think that even for oncologists or surgical oncologists or breast—or medical oncologists, it's really important to think about this. That could be prevention of a second breast cancer, and we know that second cancers are the most common category of cancers for individuals with a first cancer, so thinking about that is really, really important. We tend to not think about prevention in our desire to treat and eradicate the disease, but prevention is going to be key to this.

Dr. Sands:
With that insightful information in mind, I want to thank my guest, Dr. Marie Wood, for sharing her insights on chemoprevention for patients at high risk of breast cancer. Dr. Wood, thank you so much for being here today.

Dr. Wood:
It's really been a pleasure.

Dr. Sands:
I'm Dr. Jacob Sands. To access this and other episodes in our series, visit reachmd.com/projectoncology, where you can be Part of the Knowledge. Thanks for listening.