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Rethinking Cancer Screening: The Rationale for Multi-Biomarker MCED Testing

Announcer:
You're listening to *Project Oncology* on ReachMD, and this episode is sponsored by Exact Sciences. Here's your host, Dr. Brian McDonough.

Dr. McDonough:
This is *Project Oncology* on ReachMD, and I'm Dr. Brian McDonough. Joining me to discuss the rationale for using a multi-biomarker approach to multi-cancer early detection, or MCED, testing is Dr. Marie Wood. Not only is she a board-certified medical oncologist and Professor of Medicine at the University of Colorado School of Medicine, but she's also Medical Director of the Hereditary Cancer Program at the CU Cancer Center. Dr. Wood, thanks for being here today.

Dr. Wood:
It's a pleasure to join you today. Thank you for inviting me.

Dr. McDonough:
So, Dr. Wood, let's start by looking at a big picture here. Traditional cancer screening has always been organ specific. We look at one specific organ, but now we have MCED testing. What does that bring to the table?

Dr. Wood:
So I think it has a lot of promise. As you probably know, cancer screening is fraught with issues. Right now, we have guidelines for separate cancers; that screening starts at different ages, and it involves different technologies, ranging in invasiveness. We know there are issues with adherence and access to care. Wouldn't it be great if we could just do a single blood test and find cancer? So I think that's the promise.

Dr. McDonough:
So with that background in mind, let's zero in on the different types of MCED testing. How do single biomarker tests work? And do they have any limitations we should know about?

Dr. Wood:
Single biomarkers just look for a single protein or specific change. In the multi-cancer early detection tests or multi-cancer detection tests, we're looking at a lot of different biomarkers. This could be circulating DNA. This could be methylation pattern. The companies that are developing these tests are using a range of technology. The data all comes in, and then they use machine learning algorithms to integrate the data, sometimes adding additional testing to develop the signal—positive or negative—and the tissue of origin.

Dr. McDonough:
So I can see some limitations with the single biomarker. But then again, as you're talking about it, there's pluses in the multi-biomarker model as well, and they're kind of figuring it out?

Dr. Wood:
I think there are a lot of studies out there that are looking at populations of patients with cancer and patients without cancer. When they

interrogate these tests on those populations, they are able to identify signals in many of the cancers for which we don't have screening today, such as pancreatic cancer, esophageal cancer, and ovarian cancer. They oftentimes have a harder time detecting things like prostate cancer or breast cancer—cancers that don't often shed.

The other thing that is a limitation of these tests is that they're much more accurate at identifying stage 3 or 4 cancers as opposed to stage 1 or stage 2 cancers. So if we're going to really use this technology for early detection, you want to find cancer when it's at early stage. Let's take the example of ovarian cancer. There's a lot of tests that have been done looking for ovarian cancer screening, but to date, we don't have cancer screening because we can't find the cancer early. So if this technology really does find cancer early, then it can be used in conjunction with standard screening.

Dr. McDonough:
For those just tuning in, you're listening to *Project Oncology* on ReachMD. I'm Dr. Brian McDonough, and I'm speaking with Dr. Marie Wood about single versus multi-biomarker approaches to MCED testing.

You brought up a really interesting point, I think, Dr. Wood, talking about ovarian cancer. That's always frustrating for all of us because I know we've had markers we look for but they're not specific, and then somebody might have bloating as a symptom, and that could be your only warning sign. And then by the time you get to the ovarian cancer and try to treat it, it's already progressed.

I think that's what you're getting at here. And you're hoping that maybe with different cancer types they're looking at and all these things, we might have better shots at getting at these—is that kind of what we're hoping?

Dr. Wood:
I think that's the promise of the technology. I don't think we're there yet. I think we have a ways to go. I should point out some of the other issues with these tests: they can be falsely positive or falsely negative.

So falsely positive means you get a blood test, your primary care provider or whoever orders it tells you the test is positive. You move on to try and figure out what cancer you have and where it is, and despite sometimes multiple months of testing, cancer is never found. So that would be a false positive test. And that does happen with these tests.

So I think that there are a couple things that can cause false positives. As I mentioned, we're looking for circulating DNA or methylation patterns of DNA. So certain diseases like clonal hematopoiesis, which causes abnormal DNA signals but is not necessarily a diagnosis of cancer, have to be ruled out. There are also other inflammatory conditions that, as you might imagine, can alter DNA patterns. The companies often do a fairly good job of ruling those out, but that is an issue.

Also, as I mentioned, that diagnostic evaluation or diagnostic journey can take many months. And what do you do if still at the end of it, you don't have cancer? So I think if you get a false positive result and you can't find cancer, then I think a primary care provider should talk to their patient and probably test again in another year.

So this is one technology and one potential avenue. I think we have to be careful of primary care providers or patients saying, 'Oh, I have a single test. I don't need my colonoscopy. I don't need to do anything for a couple of years,' because this is just one test. And we're not yet sure how to put it in context with what we know is current cancer screening. But it certainly does have a lot of promise.

Dr. McDonough:
If we focus on these tests and how they're designed, what makes a multi-biomarker test scientifically rigorous and clinically practical? I know you were just talking about the practicality of it.

Dr. Wood:
Yeah, I think that "scientifically rigorous" means that you can detect cancer, but what does that mean? So there's a positive signal, but that has to correlate with finding a cancer.

So I think that we have the technology. We can find circulating DNA in blood. Sometimes that can identify a cancer signal, but I think we have to do some rigorous clinical trials to figure out, is this identifying early-stage cancer or is it late-stage cancer? And is this better than our current screening paradigm? Which, as I mentioned, tests for multiple cancer using multiple different technologies.

Dr. McDonough:
You brought up a lot of the pros, a lot of the concerns, and a lot of the scientific investigation. So before we wrap up, Dr. Wood, let's look ahead for a moment. How do you see these kinds of MCED tests influencing future innovation in this space as we move forward?

Dr. Wood:
So to answer your question, which I think is so important, these tests have great promise, but we need to know that they're clinically actionable. We need to know how to integrate them in what we know today for current cancer screening.

The tests that have previously been done have largely been done in very homogeneous populations. There is a large clinical trial that is just being launched in the United States that will test thousands of individuals with these tests and follow their results. They're really trying to recruit a diverse population. If these tests are going to be good, they need to reach everybody. They need to be covered by insurance, and we need to know how to integrate them into the population and into what we already know.

Another example is if you get a positive test—a test that insurance doesn't cover and costs about $1,000—then you have to still do an evaluation. That evaluation can be PET scans, CAT scans, bone marrow biopsies, and other biopsies. Who's going to cover that evaluation?

A lot of these things need to be worked out. And that's why I'm very excited about this study that will really help us figure out how to put this in the context of what we already know about screening.

Dr. McDonough:
Well, as those forward-looking thoughts bring us to the end of today's program, I want to thank my guest, Dr. Marie Wood, for joining me to discuss a multi-biomarker approach to MCED testing. Dr. Wood, it was wonderful having you on the program.

Dr. Wood:
Thank you, and thank you for inviting me.

Announcer:
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