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**ReachMD**
www.reachmd.com
info@reachmd.com
(866) 423-7849

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Multi-Cancer Early Detection: Framing the Future of Cancer Screening

**Announcer:**
Welcome to ReachMD.

This medical industry feature, titled "Multi-Cancer Early Detection: Framing the Future of Cancer Screening," is sponsored by Exact Sciences.

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Here's your host, Dr. Charles Turck.

**Dr. Turck:**
According to the CDC, rates of patients who get screened for cancer have declined over the past decade, but emerging research on a new tool for cancer screenings may not only help us improve these rates but also help us detect cancer earlier. This is ReachMD, and I'm Dr. Charles Turck. Joining me to discuss the future of cancer screenings and their impact on early detection is Dr. Tom Beer, who is an Adjunct Professor of Medicine in the Division of Hematology and Medical Oncology at Oregon Health and Science University and Chief Medical Officer for Multi-Cancer Early Detection at Exact Sciences Corporation. Dr. Beer, welcome to the program.

**Dr. Beer:**
Great to be with you.

**Dr. Turck:**
To start us off, Dr. Beer, can you tell us about the progress the United States has made in cancer detection and prevention so far?

**Dr. Beer:**
Over the last several decades, we've developed strong evidence of cancer-specific survival benefit for early detection for four individual cancers – cervical, colorectal, lung, and breast – and perhaps there's no better example of the impact of early detection than cervical cancer where there's been a dramatic reduction in mortality from cervical cancer over the last several decades as screening has become widespread and, more recently, an HPV vaccine has become available. Indeed, the American Cancer Society recently launched a roundtable on cervical cancer effort whose goal is the eradication of cervical cancer, so that is a powerful example of what early detection can do. At the same time, we've only been able to develop four standard of care cancer screening strategies for four cancers. These are some of the most common cancers, but it leaves more than ~70%*[.3] of cancer deaths due to cancers for which we do not currently have any standard of care screenings. So, that's where the greatest need is today, and that need and opportunity has been widely recognized, including by the White House Moonshot program whose goal is to reduce mortality from cancer overall by half over the next 25 years, and the Moonshot program has identified cancer early detection, particularly the early detection of these cancers for which we currently do not have standard of care screening tests, as a major opportunity to drive towards that goal of reducing cancer mortality by half in the next two and a half decades.

**Dr. Turck:**
With that background in mind, have there been any advancements in science and technology that are working to address these needs?

**Dr. Beer:**

Indeed, there have been significant advances in science and technology that enable us to contemplate entirely new approaches to cancer early detection today. That really begins with the fundamental understanding of cancer biology that has been developed over several decades across countless research institutions all around the world. That understanding has taught us the biologic underpinnings of cancer – things like DNA mutations, gene silencing through DNA methylation, alterations in the structure of chromosomes and the presence of abnormal proteins that contribute to the growth and aggressiveness of cancer. That cancer biology then enables us to look for these hallmarks of cancer with new diagnostic tests. These tests in turn are enabled by analytic and diagnostic technologies that have evolved over the last number of years – technologies that enable us to, at a very high level of sensitivity, search for unique DNA sequences that carry cancer mutations and are detectable in the blood. We can also detect these other hallmarks that we discussed – DNA methylations, alteration in chromosomal structure, proteins, and other so-called biomarkers or biomarker classes – with highly sensitive diagnostic technologies. So, the combination of understanding what drives cancer and technological advances that enable high sensitivity blood tests to pick up those cancer signals is what's enabling breakthrough approaches to cancer early detection. What we're focused on at Exact Sciences in this field is primarily multi-cancer early detection, designed to complement single-cancer early detection tests. These multi-cancer early detection tests, also known as MCED TESTs, are designed to pick up these early cancer signals in the blood and enable us to detect multiple cancers from a single blood test simultaneously. The research that's gone into that work, has come from many institutions. At Exact Sciences, the technologies we're working on came out of primarily Johns Hopkins and the Mayo Clinic and have been evolved in the laboratories at Exact Sciences.

**Dr. Turck:**
Speaking just a little bit more about MCEDs, what else does our initial research tell us about this type of test?

**Dr. Beer:**
So, at Exact Sciences, we carried out the first prospective clinical trial of a multi-cancer early detection test. The trial was called DETECT-A, and the prototype MCED test was called CancerSEEK. The technology for the CancerSEEK test came out of laboratories at Johns Hopkins and focused on an analysis that sought to identify cancer-related mutations and abnormal cancer-related proteins in the blood of patients or, really, people seeking screening. They weren't patients at that time. The study enrolled more than 10,000 women between the ages of 65 and 75 and completed enrollment in 2019, results being published in 2020.[2] So, this landmark study demonstrated several key things. First of all, a single blood test was able to detect cancer and was able to detect cancers early. About two-thirds of the cancers detected as a consequence of the blood test were in the pre-metastatic phase when they would not have been picked up clinically. Secondly, the application of this blood test more than doubled the proportion of cancers detected through a screening test, and that's truly a remarkable result. In that study, about a quarter of cancers were detected through a standard of care screening test, things like mammography or cervical cancer screening or colorectal cancer screening, but when combined with the blood test, that needle was moved from about a quarter to more than half. More than half the cancers in DETECT-A were diagnosed not because of a clinical presentation of symptoms of cancer but through the use of an early cancer detection test. Finally, what DETECT-A showed us is that an imaging-based diagnostic approach to those patients whose blood test signals the possibility of cancer was both efficient and effective at ruling in or ruling out the presence of cancer. So, it is those data that enable us now to move forward and continue to refine and develop the next generation of multi-cancer early detection tests.[2]

**Dr. Turck:**
For those just tuning in, you're listening to ReachMD. I'm Dr. Charles Turck, and today I'm speaking with Dr. Tom Beer about the progress of early cancer detection through screenings.

Now, Dr. Beer, let's shift our attention to MCEDs' impact on health equity. How can this type of test potentially close the gap of health equity disparities?

**Dr. Beer:**
This is a critically important question. As you know, we face an epidemic of cancer. We have 1.9 million new cancers diagnosed in the United States every year, and more than 600,000 people die due to cancer in the United States every year.[3] That burden of cancer is not distributed equally across society, with a number of groups suffering disproportionately.[3] So, we need to be working hard to close those gaps in cancer burden. We also need to be mindful that any new technology can exacerbate rather than reduce disparities if it's not introduced broadly to all groups affected by cancer. The potential advantage of MCED tests is that they are a single blood test for multiple cancers and therefore they're easy to implement and should be accessible in almost any setting in the United States. Blood tests are nearly universally accessible across this country, including in areas where access to care in general, is not as robust as in the rest of the country. We do need to be thoughtful about what it takes, though, because it's not just a blood test it's also the diagnostic evaluation that follows – and so as we implement MCED tests across communities in the United States and pay attention to make sure that they're available everywhere, we also need to make sure that those folks who receive a signal from their MCED test have access to

the necessary imaging evaluation to follow up on that test, and that's a critical priority for the field.

**Dr. Turck:**
And what are some key strategies you would recommend for clinicians hoping to implement MCED tests into their practice?

**Dr. Beer:**
Sure. So, first of all,I want to acknowledge that it's still early days in MCED test development when it comes to clinical implementation. That's not to say that the work on these tests just began recently. Indeed, the work has been going on for more than a decade at many academic institutions, and the foundations for the work that we're doing at Exact Sciences came out of the laboratories at Johns Hopkins and the Mayo Clinic that has continued in the laboratories at Exact Sciences, but in terms of clinical implementation, we're still gathering data on safety and efficacy of these tests. Right now, what we are clear on is that these tests are designed as a complement and not as a replacement for standard of care screening, and that's a critically important point. The standard of care screening tests that we have available today have proven benefits in terms of cancer-specific survival for cervical, lung, colorectal, and breast cancer. MCED tests are primarily designed to complement those and extend the potential of screening to all the other cancers but not to replace them. We're also really thinking differently about MCED tests than about current, single-cancer screening tests. We're looking at these tests as screening individuals for cancer and not screening people for individual cancers, and so there's really a mind shift when we start thinking about implementing multi-cancer early detection.

The other thing that's important to know as we consider these tests in clinic is that their design is a little bit different. Single-cancer screening tests are designed to have a high sensitivity to detect as many cancers as possible and accept a relatively low specificity, meaning that false positives are pretty common, and if you look at the performance of current mammography or various colorectal screening tests, certainly lung cancer CT, we've accepted the fact that we may get a positive signal, and quite frequently, in fact, in a large majority of patients, follow-up tests do not reveal a cancer. With multi-cancer early detection, we're really calibrating them differently and emphasizing specificity in order to reduce false positives because we recognize that a false positive multi-cancer early detection test requires an extensive evaluation, can induce worry and anxiety, and we want to limit that, but along with that comes a planned feature of a somewhat lower sensitivity. So, we need to be mindful that a negative MCED test is not tantamount to a clean bill of health. It is a result that is important and, tells the patient that a work-up is not necessary, but it does not get us off the hook of the vigilance necessary with standard of care screening tests. It does not rule out the presence of cancer.

**Dr. Turck:**
Looking to the future, Dr. Beer, what's on the horizon for MCED testing?

**Dr. Beer:**
Well, at Exact Sciences, we have built on the results of DETECT-A, added biomarker classes in order to further improve the performance of the test, and looking ahead, we are finalizing the work necessary to lock down the best possible assay using samples from so-called case-control studies – samples collected for patients with a known cancer diagnosis and from participants thought to be cancer-free.[1] We're looking ahead to launching prospective clinical trials to further evaluate our multi-cancer early detection test in the general average-risk population that would be potentially amenable to cancer screening using an MCED test, and we see a lot of promise in the development of MCED tests, primarily as a complement to standard of care.

Screening tests designed to markedly expand access to screening and address the 70% of cancer deaths that are occurring due to cancers that currently have no standard of care screening at all. And, we hope with the research that we have planned, as well as real-world evidence gathering efforts using a laboratory-developed test, that we intend to bring forward, we will contribute to the White House Cancer Moonshot goal of reducing cancer mortality by half or more in the next 25 years.

**Dr. Turck:**
Those are great insights for us to think on as we come to the end of today's program. I want to thank my guest, Dr. Tom Beer, for helping us better understand the potential approach to multi-cancer early detection screenings. Dr. Beer, it was great speaking with you today.

**Dr. Beer:**
Thank you so much.

**Announcer:**
This program was brought to you by Exact Sciences. If you missed any part of this discussion, visit ReachMD dot com slash industry feature. This is ReachMD. Be Part of the Knowledge.

*U.S. Data. Calculated using estimated new cases of cancers that have standard of care screening: breast, cervical, colorectal and lung

(high-risk for each sex) against all sites

**References**

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