Supporting the Use of a Blood Test for Early Detection of Multiple Types of Cancer

Summary of "Prognostic Significance of Blood-Based Multi-cancer Detection in Plasma Cell-Free DNA"
– Data published in *Clinical Cancer Research*, 2021 –

Detecting cancer early, when it is easiest to treat, gives patients the best chance of surviving.[1-3] That's why doctors screen for some of the most common cancers, such as breast or colorectal. While screening saves lives, it is only recommended for five cancer types and current screening tests only look for one type of cancer at a time. But there are many other types of cancers that *don't* have screening tests. In fact, approximately two-thirds of all cancer deaths are from cancers that lack any recommended screening today.[4] So, what if we could look for many types of cancer all at once in a way that is safe for patients?

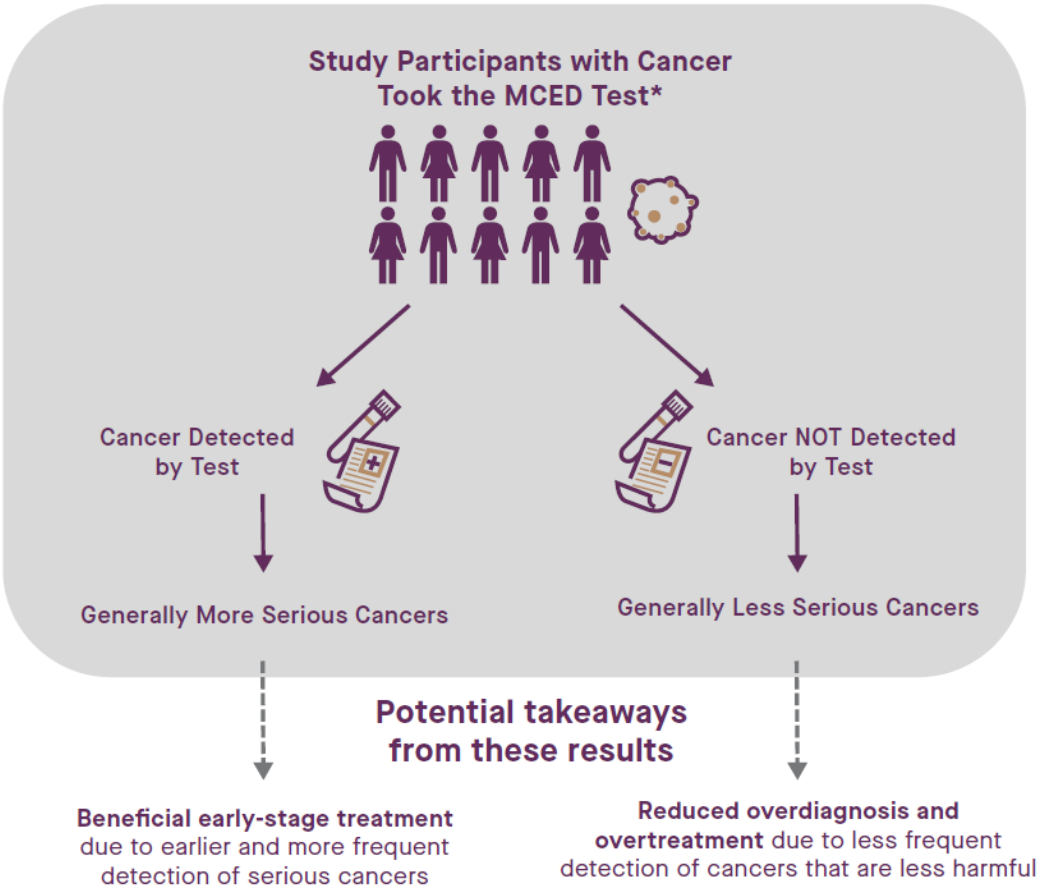
A new multi-cancer early detection (MCED) test has been developed by GRAIL that can detect many cancer types with a single blood draw.[5] It does this by using technology to look at small pieces of DNA that cancer cells shed into the blood. These small pieces are called circulating tumor DNA, or "ctDNA" for short. The test also uses ctDNA patterns to predict where the cancer is located in the body. This is important to help doctors recommend next steps for follow-up testing.[6]

In this study, one of the things researchers wanted to check was whether a version of the MCED test could detect dangerous cancers. They also wanted to confirm that the test did not detect many cancers that do *not* cause serious harm during a patient's lifetime. Finally, they wanted to understand how the amount of ctDNA in the blood was related to cancer severity. To answer these questions, a study was conducted in over 2,000 participants with cancer in the United States and Canada.[7] The study participants took the MCED test and were followed for up to 3

years. The goal of this analysis was to better understand how the MCED test performed in people with cancer, not to use the MCED test to help guide cancer treatment. For this reason, MCED test results were not sent to the participants' physicians. Therefore, any cancer treatment participants received during the study were not based on their MCED test results.

The first thing the researchers looked at was how long the participants in the study survived. Participants whose cancer was *not* detected by the MCED test had better chances of surviving than participants whose cancer *was* detected by the test (Figure). This was true in early, mid, and late cancer stages. This means that the MCED test detected cancers that are more life-threatening and did not detect as many cancers that are less harmful. These results are important for two reasons. First, the MCED test can detect serious cancers more frequently and earlier, so patients can receive beneficial early-stage treatment. Second, it can reduce unnecessary follow-up testing and treatment in people with cancers that are less serious and less likely to require immediate care. It is important to note that these results do not mean that the MCED test has the ability to detect *all* aggressive cancers. Also, like all detection tests, there is a chance that the MCED test may incorrectly detect a cancer signal in a patient who does not have cancer.

MCED Test Detected More Life-Threatening Cancers



*MCED test results were not used to influence treatment decisions.
MCED, multi-cancer early detection.

Researchers found that for study participants with cancer detected by the MCED test, survival was similar to what you would expect in the real world. For participants with cancer that was not detected by the MCED test, survival was better than expected in the real world. This confirmed that less harmful cancers were not being detected as frequently with the MCED test. It is important to remember that the MCED test results in this study were not used to influence treatment decisions. Future research will study how early detection of cancer using the MCED test can improve chances of survival.

The final question researchers wanted to know was if the amount of ctDNA in the blood was related to cancer severity. A higher amount of ctDNA in the blood was generally seen in later stage cancers. Participants with a lower amount of ctDNA in the blood also had better survival than those with more ctDNA. This demonstrates that the amount of ctDNA may indicate the severity of the cancer. Results also found detection rates increased in cancers with higher ctDNA levels, and those in later stages. This suggests that this MCED test detected aggressive cancers and did not detect as many slow-growing cancers. Therefore, the test is unlikely to contribute to overdiagnosis or overtreatment.

Taken together with results from other studies, these results show that the MCED test may serve as a valuable tool to detect serious cancers early when treatment may be most effective.

Published Article: https://clincancerres.aacrjournals.org/content/27/15/4221
Authors: Xiaoji Chen, Zhao Dong, Earl Hubbell, Kathryn N. Kurtzman, Geoffrey R. Oxnard, Oliver Venn, Collin Melton, Christina A. Clarke, Rita Shaknovich, Ting Ma, Gerry Meixiong, Michael V. Seiden, Eric A. Klein, Eric T. Fung, and Minetta C. Liu

References

1. Siegel, R. L., et al. *Cancer J. Clin.* 2018;68(1):7–30 https://acsjournals.onlinelibrary.wiley.com/doi/full/10.3322/caac.21442
2. Ahlquist DA. Universal cancer screening: revolutionary, rational, and realizable. *Npj Precis Oncol* 2018;2:23. https://www.nature.com/articles/s41698-018-0066-x
3. Hawkes N. Cancer survival data emphasise importance of early diagnosis. *BMJ*. 2019;364:l408.
4. Estimated deaths per year in 2021 from American Cancer Society Cancer Facts and Figures 2021. Available at: http://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/annual-cancer-facts-and-figures/2021/cancer-facts-and-figures-2021.pdf. Data on file GA-2021-0065.
5. https://www.galleri.com/
6. Liu MC, et al. Sensitive and specific multi-cancer detection and localization using methylation signatures in cell-free DNA. *Ann Oncol*. 2020;31(6):745-759.
7. Chen X, et al. Prognostic Significance of Blood-Based Multi-cancer Detection in Plasma Cell-Free DNA. *Clinical Cancer Research*. 2021;27(15):4221-4229. doi: 10.1158/1078-0432.CCR-21-0417.