New ultra-sensitive blood test predicts recurrence of breast cancer, months or years before relapse

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Dr Isaac Garcia-Murillas. Credit: Institute of Cancer Research

A new type of blood test can predict the recurrence of breast cancer in high-risk patients, months or even years before they relapse, research has shown.

A team from The Institute of Cancer Research, London, used an ultra-sensitive liquid biopsy to detect the presence of tiny amounts of cancer DNA left in the body following treatment for early breast cancer.

The findings, presented at the American Society of Clinical Oncology (ASCO) annual meeting in Chicago on Sunday 2 June, involved analyzing blood samples from the ChemoNEAR sample collection study for circulating tumor DNA (ctDNA) that is released into the bloodstream by cancer cells.

The researchers, based at the Breast Cancer Now Toby Robins Research Center at The Institute of Cancer Research (ICR), were able to identify all patients from the study who later went on to relapse by detecting very low levels of cancer found in the blood—known as molecular residual disease.

Detecting larger numbers of cancer-related changes

By helping to spot the patients most likely to relapse, the ICR scientists hope the results will pave the way for a new strategy for treating recurrent breast cancer where treatment can be started much earlier, without waiting for incurable, advanced disease to develop and show up on a scan.

Although previous studies have shown that ctDNA blood tests can identify relapse long before it can be seen on a scan, most tests use a technique called whole exome sequencing (WES) as it focuses on the exons—the protein-coding regions of genes—which are directly related to diseases.

However, the approach in this study, involves sequencing the entire genome, known as whole genome sequencing (WGS). This enabled researchers to identify up to 1,800 mutations, which is much more

sensitive and includes a larger number of cancer-related changes that could occur in a patient's DNA.

Blood samples from 78 patients with different types of early breast cancer (23 with triple negative breast cancer, 35 with HER2+ breast cancer, 18 with hormone receptor+ breast cancer and two with an unknown subtype) were screened for ctDNA.

The samples were collected from the women at diagnosis before their therapy, after the second cycle of chemotherapy, following their surgery and every three months during follow-up for the first year. After that, samples were collected every six months for the next five years.

Spotting which patients are most likely to relapse

The results showed that detection of ctDNA at any point after surgery or during the follow up period was associated with a high risk of future relapse and poorer overall survival.

Molecular residual disease was detected in all 11 patients who relapsed. The median lead time to clinical relapse in this group of patients was 15 months, an increase of over three months, compared with current tests in all types of breast cancer. The longest lead time to clinical relapse was 41 months.

None of the 60 women in whom ctDNA remained undetected, relapsed throughout the follow-up period. Three patients had ctDNA detected in follow-up but had not relapsed by the end of the study—the researchers didn't have samples to analyze beyond the study follow-up period. Median survival for ctDNA detected patients was 62 months and not reached for the patients in whom ctDNA was undetected.

"This proof-of-principle retrospective study lays the groundwork for

better post-treatment monitoring and potentially life-extending treatment in patients."

First author, Dr. Isaac Garcia-Murillas, Staff Scientist in the Molecular Oncology Group at The Institute of Cancer Research, London, said, "Breast cancer cells can remain in the body after surgery and other treatments but there can be so few of these cells that they are undetectable on follow-up scans.

"These cells can cause breast cancer patients to relapse many years after their initial treatment. Ultra-sensitive blood tests could offer a better approach for the long-term monitoring of patients whose cancer is at high risk of returning.

"Most personalized liquid biopsies currently use whole exome sequencing to identify mutations. But this approach goes one step further and uses whole genome sequencing to identify up to 1,800 mutations in a patient's tumor DNA that could uniquely identify recurrence of the patient's cancer from a blood sample.

"A more sensitive test is very important for this group of early breast cancer patients as they tend to have a very low amount of cancer DNA in their blood. This proof-of-principle retrospective study lays the groundwork for better post-treatment monitoring and potentially life-extending treatment in patients."

Professor Nicholas Turner, Professor of Molecular Oncology at the ICR, and Consultant Medical Oncologist at The Royal Marsden NHS Foundation Trust, said, "Testing a patient's blood for ctDNA will allow clinicians to diagnose the return of cancer at the very earliest stage. However, further research and testing are needed before we can demonstrate whether detecting molecular residual disease could guide therapy in the future.

"The ongoing TRAK-ER trial at The Royal Marsden, for example, is using a different molecular test to identify circulating tumor DNA and predict relapse in ER positive breast cancer patients. This trial is looking at whether relapse in patients with residual disease could be prevented by altering their treatment."

Professor Kristian Helin, Chief Executive of the ICR, said, "Breast cancer is much easier to treat before it spreads to other parts of the body, so it is vital to be able to detect signs of recurrence of the disease as early as possible to give people the best chance of survival.

"It is very exciting to see advances in technology that can detect cancer cells and DNA with greater sensitivity to pick up residual disease or detect the early signs of breast cancer recurrence while a cure is still possible.

"These approaches are having a transformative effect on cancer diagnosis. They will help us exploit our knowledge of cancer risk to develop new strategies for targeted screening and detection."

Dr. Simon Vincent, director of research, support and influencing at Breast Cancer Now, said, "Early detection is one of our greatest weapons against breast cancer and these initial findings, which suggests new tests could be able to detect signs of breast cancer recurrence over a year before symptoms emerge, are incredibly exciting.

"While this research is still in its early stages, catching breast cancer recurrence earlier means treatment is much more likely to destroy the cancer and stop it spreading to other parts of the body, at which point it becomes incurable.

"With around 11,000 people dying every year in the U.K. from secondary breast cancer, breakthroughs like these are urgently needed so

that we can stop people losing their lives to this devastating disease.

"We look forward to seeing further findings from this promising study and encourage anyone who is affected by breast cancer to contact our helpline by calling 0808 800 6000 for information and support from our expert nurses."

Dr. Richard Chen, chief medical officer and executive vice president of R&D at Personalis, said, "We are excited to work with Professor Turner, Dr. Garcia-Murillas and other breast cancer leaders at the ICR on this ground-breaking breast cancer study.

"The study shows the importance and promise of using an ultra-sensitive MRD test like NeXT Personal to detect the earliest traces of breast cancer recurrence, and more optimally guide management of breast cancer patients."

Provided by Institute of Cancer Research

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