Test can predict how people with leukaemia will respond to chemotherapy

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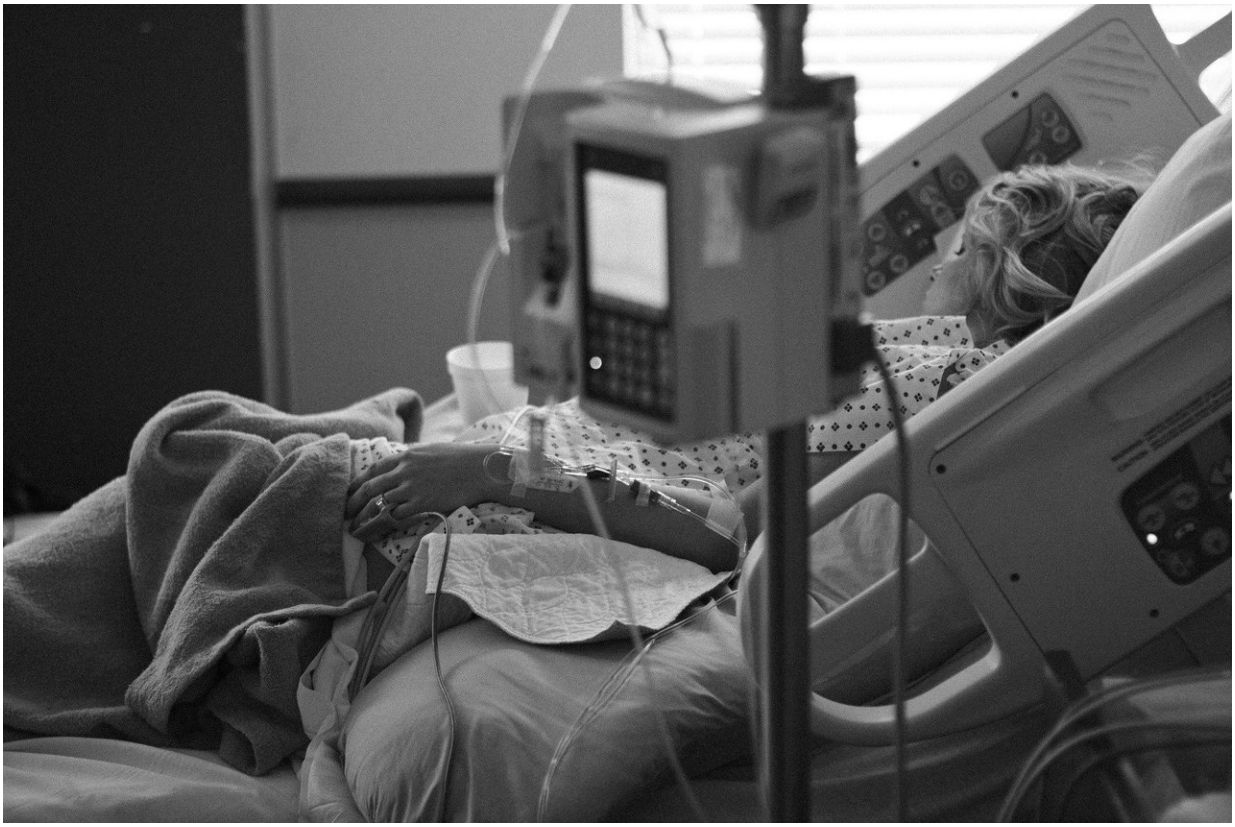

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The first test to quickly and accurately predict how people will respond to standard treatment for the most common type of leukaemia has been developed at Cardiff University. The technology could guide doctors'

decisions on which drugs to give to patients.

The Cardiff researchers say that the test could now be a 'game changer' in the treatment of chronic lymphocytic leukaemia (CLL). It also has the potential to change how other cancers, including myeloma and breast cancer, are treated. While previous versions of the test had taken a week to process, results can now be ready in a day.

The research, which was funded by the blood cancer research charity Bloodwise, is published the journal *Leukemia*.

CLL is a slowly developing blood cancer in which patients produce mutated versions of white blood cells that build up in the blood, bone marrow and lymph nodes and crowd out healthy blood cells.

CLL progresses at different rates in different people and never progresses at all in a third of patients. Until now there has been no accurate test that can be used to indicate whether and how fast individual patients' cancer will develop.

The high-throughput 'STELA' test developed in Cardiff measures the length of sections of DNA in cancer cells called telomeres, which are found at the end of chromosomes. Telomeres act in the same way as protective plastic tips on the end of shoelaces, preventing chromosomes ends from 'fraying'.

Telomeres shorten every time a cell divides to create a new cell and eventually the chromosome ends are left exposed – leading to extensive DNA damage that speeds up cancer progression.

The Cardiff researchers have shown that people who have very short telomeres when they are diagnosed are much more likely to have a fast-progressing cancer.

The improved STELA test was used to analyse samples from 260 patients to see if it could predict how patients would respond to intensive chemotherapy combined with immunotherapy. The test showed that people with short telomeres relapsed much sooner after treatment than patients with long telomeres – on average 3.7 years after treatment compared to 5.5 years.

Patients with cancer cells containing mutations to the IGHV gene are known to have a better outcome than patients without this genetic mutation. The STELA test was found to be a more accurate predictor of relapse than testing for the IGHV mutation or any other current prognostic or predictive test.

Professor Duncan Baird, who developed the test at Cardiff University's School of Medicine with Professors Chris Pepper and Chris Fegan, said: "Not all patients benefit equally from chemotherapy and this test is the only one available that can accurately predict how patients are likely to respond. Our research provides strong evidence that a significant number of patients should be receiving more appropriate treatments."

Professor Chris Pepper, who is now based at Sussex Medical School, University of Sussex, said: "Our study shows that some patients have a very long duration of response to chemoimmunotherapy, and may even be cured. These patients all have long telomeres. In contrast, patients with short telomeres invariably showed an inferior response and should be considered for alternative treatments."

Dr. Alasdair Rankin, Director of Research at Bloodwise, said: "People with CLL can experience great anxiety and uncertainty about how their cancer will progress. This test could give people the peace of mind that they will receive the most effective treatment possible if it does. It may even allow some people to be told that their cancer is unlikely to progress."

CLL is diagnosed in over 4,000 people each year in the UK and is the most common type of adult leukaemia. Patients produce immature versions of white blood cells called lymphocytes, which build up in the bone marrow and crowd out healthy blood cells.

CLL develops slowly and primarily affects patients' immune systems and their ability to fight off infections. Symptoms can include fatigue, swollen lymph nodes, frequent infections, weight loss and night sweats.

Many patients will not start treatment straight away, but will be put on a programme called 'watch and wait' until the cancer develops further. Some patients will never need treatment. For those patients who do undergo treatment, this usual consists of a combination of chemotherapy drugs and monoclonal antibody drugs—artificial antibodies that bind to and kill specific cancer cells. While current drugs are often effective at delaying the progress of the disease and patients can live for many years after treatment, CLL is currently incurable.

More information: Kevin Norris et al. Telomere length predicts for outcome to FCR chemotherapy in CLL, *Leukemia* (2019). DOI: 10.1038/s41375-019-0389-9

Provided by Bloodwise