Experimental white blood cell treatment shows 'remarkable' promise in leukaemia

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An experimental treatment that trains a patient's immune system to attack their cancer caused remission in 90 per cent of leukaemia patients on a small-scale trial, though experts warn questions remain.

The patients, who had a form of leukaemia called B cell acute lymphoblastic leukaemia (B-ALL), had been treated with several other therapies, and had exhausted all other options.

Researchers from the University of Pennsylvania used a technique called 'chimeric antigen receptor' (CAR) therapy to teach a patient's own T cells (a type of white blood cell) to recognise proteins on the surface of their cancer cells, and destroy them.

The results of the trial published in The *New England Journal of Medicine* (link is external), show that 27 of the 30 patients in the study saw a complete remission after receiving the engineered cells, and 78 per cent of the patients were alive six months after treatment.

Senior author Professor Stephan Grupp, from the University's Perelman School of Medicine, said the results were "unprecedented".

"The patients who participated in these trials had relapsed as many as four times, including 60 per cent whose cancers came back even after stem cell transplants. Their cancers were so aggressive they had no treatment options left," he said.

However, Cancer Research UK experts cautioned that, although the findings were "dramatic", the therapy was complex to perform, had serious side effects, and raised several unanswered questions.

"This study is remarkable, and induced complete remissions in patients who were regarded as incurable," said Professor Ben Willcox, director of the Cancer Immunology and Immunotherapy Centre in Birmingham.

"It shows that the CAR approach is a very powerful one, that could potentially transform the way we treat these cancers."

"However, there are still several questions to answer. It's not clear whether this represents a 'true' cure, or a bridge to other potential cures such as stem cell transplants.

"On top of this, many patients had inflammatory side effects, which ranged in severity but in extreme cases were life-threatening and required anti-inflammatory drugs," he said.

"Understanding how best to manage such potentially dangerous side effects, while preserving the anti-tumour response, is another important challenge."

The treatment involves taking T cells from patients and genetically engineering them to produce a modified protein known as a chimeric antigen receptor.

This receptor is designed to bind to a second protein, known as CD19, found on the surface of immune cells called B cells, out of which several types of leukaemia can develop.

Once the modified T cells are infused back into the patient they rapidly multiply, producing an army of tumour-killing cells that set about attacking the cancer.

This, said Professor Peter Johnson, Cancer Research UK's chief clinician, made the therapy highly complex to perform. "Although this study confirms the extraordinary power of the immune system, the technique requires major expense and infrastructure to carry out," he said.

He also highlighted the long term effects, particularly in terms of infection risk. "The power of the treatment is such that all B-cells disappear, with the consequent risk of opportunistic infection and the need for life-long immune-boosting treatments – which can be very costly too."

Of the 30 patients in the study, 19 remained in remission. Fifteen of

those 19 did so using just the CAR treatment. Seven patients relapsed, between six weeks and 8.5 months after their infusions, including three whose cancers returned as CD19-negative leukaemia that would not have been targeted by the modified cells. Understanding why, said Willcox, is a priority.

"For some patients, their leukaemia returned after the treatment, apparently because the engineered T cells were too short-lived, or the tumour cells stopped displaying the CD19 target and escaped attack. How to tackle these problems is also unclear, and poses challenges for future research," he said.

A final challenge is to adapt this tactic to other forms of cancer – something that has so far produced little success.

"We urgently need to find out which molecules - in place of CD19 - can we use with the CAR approach to safely target other, non-B cell, tumours," he said.

More information: Maude, S, et al. (2014). "Chimeric Antigen Receptor T Cells for Sustained Remissions in Leukemia" *New England Journal of Medicine*, 371 (16), 1507-1517 DOI: 10.1056/NEJMoa1407222

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