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Anti-CD47 cancer therapy safe, shows promise in small clinical trial

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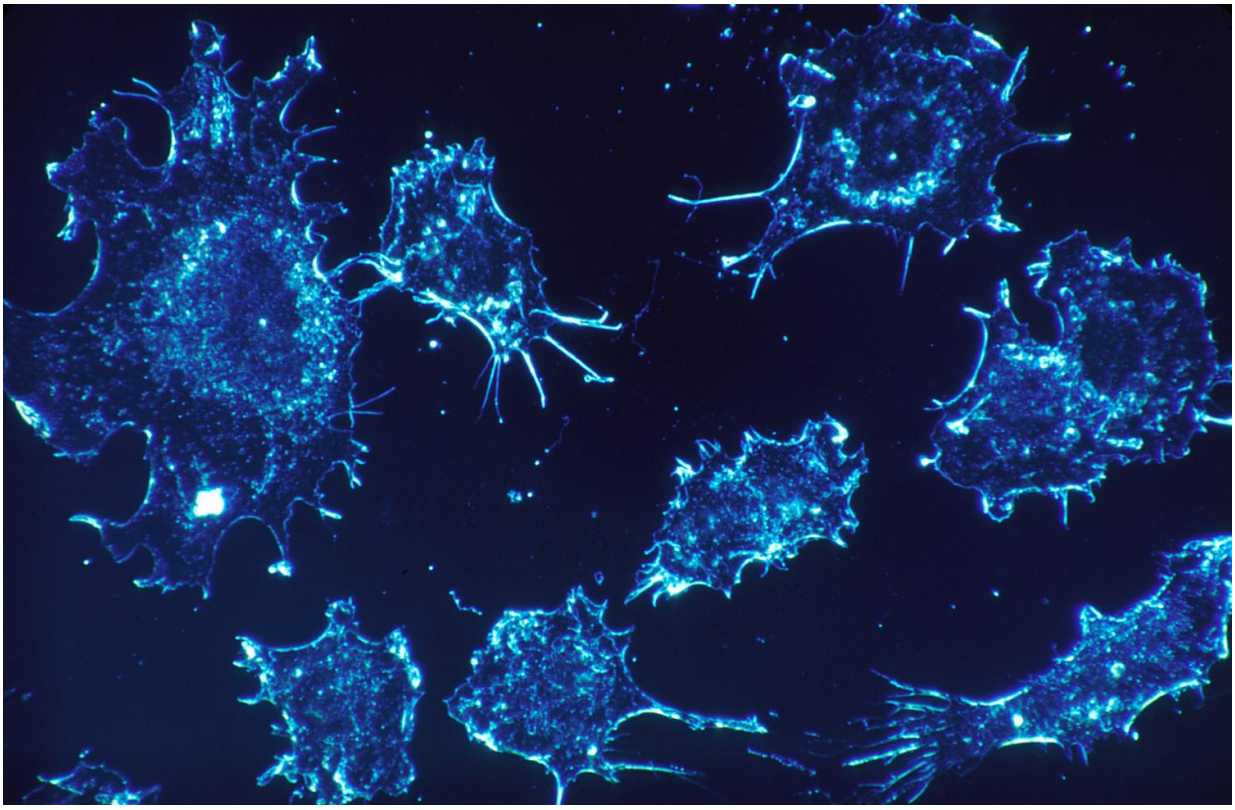

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A novel immunotherapy appears safe for use in patients with a type of blood cancer called non-Hodgkin's lymphoma, according to a phase-1 multicenter clinical trial led by a researcher at the Stanford University School of Medicine.

Although some patients showed signs of a transitory anemia or reactions at the injection site, there were few other significant side effects to the treatment, the researchers said.

The therapy combines an experimental antibody developed by researchers at Stanford and a commercially available anti-cancer antibody called rituximab. The experimental antibody, known as Hu5F9-G4, blocks the protein CD47, a "don't eat me" signal that inhibits immune attacks on cancer cells. The antibody combination was used to treat people with two types of non-Hodgkin's lymphoma: diffuse large B-cell lymphoma and follicular lymphoma.

Half of the 22 people enrolled in phase 1 of the trial had a positive response to the therapy, and about one-third went into complete remission from their cancer.

Testing for safety

Phase-1 trials are intended to test the safety of potential medical treatments in small groups of participants, but they sometimes also suggest whether a treatment is effective against specific diseases, such as cancer. Because the number of people enrolled is low, it's not possible to say definitively whether a positive result in a phase-1 trial will be echoed in future trials with larger numbers of participants.

"It was very gratifying to see how the treatment was well-tolerated and showed a clinically meaningful response," said Ranjana Advani, MD, professor of medicine at Stanford. Advani led the phase-1B clinical trial and is the lead author of a paper describing the results, which will be published Nov. 1 in *The New England Journal of Medicine*. The senior author is Sonali Smith, MD, a professor of medicine at the University of Chicago.

The clinical trial was funded by Forty Seven Inc., the company that licensed the patent from Stanford to produce Hu5F9-G4, and by the Leukemia and Lymphoma Society.

Silencing 'don't eat me' signal

In 2010, researchers led by Irving Weissman, MD, director of the Stanford Institute for Stem Cell Biology and Regenerative Medicine, showed that nearly all cancer cells cover themselves with a protein known as CD47, which acts as a "don't eat me" signal to immune cells called macrophages.

Weissman and his colleagues later developed an antibody called Hu5F9-G4 that blocks the CD47 protein, prompting macrophages to engulf and devour cancer cells. Rituximab is an antibody that has been shown to amplify positive "eat me" signals.

The combination of rituximab and Hu5F-G4 has previously been shown to work well in fighting human cancers in animal models, but this is the first published result of a clinical trial of this therapy in humans.

For this clinical trial, participants were administered a combination of Hu5F-G4 and rituximab at 10 clinical centers. All the patients in the study had failed to respond to or relapsed after at least two previous types of therapy. Hu5F-G4 was administered to the patients at slowly increasing dosages to test for adverse reactions to the antibody.

Of the 22 patients enrolled in the trial, 11 showed a clinically significant reduction in their cancers. In eight of those patients, all signs of cancer were eliminated, Advani said. Three other patients in the trial did not respond to the treatment and died due to disease progression.

Although there are many things that can kill cancer cells, the real test of

a therapy is whether it can kill the cancer cells without harming normal cells. Advani said she was particularly pleased that the researchers observed only minor side effects in the participants.

"It's very exciting to have a potentially new class of immunotherapy like this," said Advani, who is the Saul A. Rosenberg, MD, Professor of Lymphoma. "For the first time we have an antibody that activates macrophages against cancer and appears to be safe for use in humans."

Provided by Stanford University Medical Center