Cancer-Fighting Herpes Virus Shown to be an Effective Treatment for Some Advanced Melanoma

A genetically engineered herpes simplex virus, when combined with immunotherapy, reduced or eliminated tumors in one-third of patients, according to a new study.

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The herpes simplex virus type 1 (HSV-1), which affects almost two-thirds of the world's population and is generally associated with oral herpes, may cause painful cold sores or fever blisters around the mouth.

Yet, when genetically engineered to fight cancer, the virus may also play an important role in treating advanced melanoma, skin cancer that has spread to other parts of the body, according to phase 1/2 clinical trial results published in the Journal of Clinical Oncology and recently presented by Keck Medicine of USC at the 2025 American Society of Clinical Oncology annual meeting.

The study involved 140 patients from the IGNYTE clinical trial, which included Keck Medicine and other sites worldwide. These patients had advanced melanoma that did not respond or stopped responding to immunotherapy, which uses the body's own immune system to fight cancer.

Patients were treated with a genetically modified HSV-1 in combination with an immunotherapy (nivolumab). By the end of the clinical trial, one-third of the participants had their tumors shrink by at least 30%, and nearly one out of six patients had tumors completely disappear.

"These findings are very encouraging because melanoma is the fifth most common cancer for adults, and about half of all advanced melanoma cases cannot be managed with currently available immunotherapy treatments," said Gino Kim In, MD, a medical oncologist with Keck Medicine and principal investigator at the Keck Medicine clinical trial site. Dr. In is also a member of the IGNYTE trial steering committee and one of the lead investigators on the trial. "The survival rate of untreatable advanced melanoma is only a few years, so this new therapy offers hope to patients who may have run out of options to fight the cancer."

A novel class of drugs to fight cancer

The genetically modified HSV-1 evaluated in the study, RP1, is one of a relatively new, innovative class of cancer immunotherapy drugs known as oncolytic viruses that are designed to target and destroy cancer tumors while generating an anti-tumor immune response throughout the entire body. RP1 does not cause herpes.

In January 2025, the U.S. Food and Drug Administration granted priority review to RP1 with nivolumab for patients with advanced melanoma whose cancer had not responded to prior immunotherapy.

When injected into a tumor, RP1 replicates, killing off the cancer cells while leaving healthy cells unharmed. Additionally, RP1 stimulates the body's white blood cells to seek out and destroy any other cancer cells in the body.

The second cancer drug used in the study, nivolumab [Opdivo], is a standard immunotherapy treatment in fighting advanced melanoma and other cancers that have spread through the body. Researchers theorized that nivolumab, which works by using the body's own immune system to fight and destroy cancer cells, would enhance the potential effect of RP1.

How the treatment was administered

Patients admitted into the study had already been treated with minimal success by one or more immunotherapy therapies and had to have more than one tumor that could be injected with RP1. Some tumors were considered "superficial" — meaning visible on the skin, or just below the skin's surface — and some were located deeper in the body, such as in the liver or lungs. Researchers injected both superficial and deep tumors with RP1.

Encouraging findings

During the clinical trial, patients were given a combined therapy of RP1 and nivolumab every two weeks for up to eight cycles. If patients responded to the treatment, they continued on nivolumab alone every four weeks for up to 30 cycles (or two years).

Researchers measured both treated tumors and untreated tumors. They discovered that not only did injected tumor size shrink in one third of the patients by 30%, but that patients' *uninjected* tumors also shrank or even disappeared, just as frequently and as deeply.

"This result suggests that RPI is effective in targeting cancer throughout the entire body and not just the injected tumor, which expands the potential effectiveness of the drug because some tumors may be more difficult or impossible to reach," said Dr. In, who is also a member of USC Norris Comprehensive Cancer Center, part of Keck Medicine of USC.

The study also found that RP1 was well-tolerated and had a favorable safety outcome.

While it is too soon to tell if the positive outcomes remain permanent, Dr. In is optimistic about the future of RP1 therapy. "I believe that oncolytic viruses will open up an important new approach to

fighting cancer in some patients in the near future," he said.

Other clinical trial researchers include Phillip M. Cheng, MD and Ali Rastegarpour, MD, diagnostic radiologists with Keck Medicine.

Phase 3 clinical trial now open

Phase 1/2 of the IGNYTE clinical trial examined the safety, side effects, best dosing and effectiveness of administering RP1 along with nivolumab on a limited patient population. Dr. In and his fellow researchers have launched the phase 3 trial, known as IGNYTE-3, to confirm their findings in a global population of more than 400 participants.

Keck Medicine will again be one of the sites of the clinical trial, with Dr. In heading up the site. Patients interested in participating can contact Sandy Tran at sandy.tran@med.usc.edu.

Replimune, a manufacturer of RP1 and other oncolytic immunotherapies, is the sponsor of the IGNYTE clinical trial.

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