Personalized Vaccine May Help Prevent Kidney Cancer Recurrence

None of the nine patients who received the vaccine after surgery experienced recurrence over three years.

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A customized kidney cancer vaccine made from patients' tumors was well tolerated and appeared promising in a small study, according to findings published in Nature. These early findings add to the growing evidence that therapeutic vaccines could play a role in controlling cancer.

"The idea behind this trial was to specifically steer the immune system toward a target that is unique to the tumor," David Braun, MD, PhD, of Yale Cancer Center, said in a news release. "For patients with high-risk clear cell renal cell carcinoma, we want to improve post-surgery treatment options that reduce the risk of the cancer coming back."

In a Phase I trial (NCT02950766), Braun and colleagues tested a personalized neoantigen vaccine in nine people with advanced or metastatic (Stage III or IV) clear cell renal cell carcinoma (RCC), the most common type of kidney cancer. Patients' tumors were surgically removed, but they were considered to be at high risk for recurrence. Standard treatment for such patients is Keytruda (pembrolizumab) immunotherapy after surgery, but about two thirds will relapse.

Personalized cancer vaccines train the immune system to recognize specific neoantigens—abnormal proteins that distinguish cancer from normal cells—from an individual's tumor. To produce the vaccine, scientists first sequence a sample from a surgically removed tumor and use algorithms to select neoantigens that seem most likely to elicit a robust immune response. They then make a customized vaccine for each patient that delivers these proteins. Compared with some other cancers, such as melanoma, RCC has relatively few targetable mutations to work with.

"We pick targets that are unique to the cancer and different from any normal part of the body, so the immune system can be effectively 'steered' towards the cancer in a very specific way," Braun said in another news release. "We learned which specific targets in the cancer are most susceptible to immune attack and demonstrated that this approach can generate long-lasting immune responses, directing the immune system to recognize cancer."

Following surgery, customized peptide vaccines were produced for each patient. They received a

series of initial doses on days 1, 4, 8, 15 and 22—split into intradermal and subcutaneous injections—followed by two boosters at weeks 12 and 20. Five of the nine also received the checkpoint inhibitor Yervoy (ipilimumab), which unleashes T-cell activity.

After a median follow-up of about three years post-surgery, none of the nine participants had experienced kidney cancer recurrence. All of the patients generated T-cell immune responses against the neoantigens in the vaccine—including some known mutations that drive RCC growth—and seven of them showed T-cell reactivity against cells from their own tumors in the laboratory. These T cells persisted at high levels throughout follow-up. Outcomes were similar regardless of whether patients added Yervoy.

“We observed a rapid, substantial and durable expansion of new T-cell clones related to the vaccine,” said study coauthor Patrick Ott, MD, PhD, of Dana-Farber Cancer Institute. “These results support the feasibility of creating a highly immunogenic personalized neoantigen vaccine in a lower mutation burden tumor and are encouraging, though larger scale studies will be required to fully understand the clinical efficacy of this approach.”

The vaccine was safe and well-tolerated. Some people experienced local reactions at the injection site or flu-like symptoms, but there were no serious adverse effects.

“Our results demonstrate that neoantigen-targeting personalized cancer vaccines in high-risk RCC are highly immunogenic, capable of targeting key driver mutations and can induce antitumor immunity,” the study authors concluded. “These observations, in conjunction with the absence of recurrence in all nine vaccinated patients, highlights the promise of personalized cancer vaccines as effective adjuvant therapy in RCC.”

The researchers are now testing a messenger RNA (mRNA) kidney cancer vaccine, dubbed V940 or mRNA-4157, plus Keytruda in a larger Phase II trial (NCT06307431) of more than 200 patients, in collaboration with Merck and Moderna.

These results add to a growing body of evidence that therapeutic vaccines could be part of the future armamentarium to fight cancer. For example, researchers have reported promising results for personalized mRNA vaccines for melanoma and pancreatic cancer. So far, vaccines appear to work better at keeping residual cancer in check after tumors have been removed or other types of treatment have brought about remission, rather than eliminating large established tumors.

In addition to personalized neoantigen vaccines that train the immune system to recognize an individual’s tumor, researchers are also studying off-the-shelf vaccines that use antigens, such as HER2, that are shared by people with the same type of cancer. Note that these therapeutic, or treatment, vaccines are different from existing preventive vaccines that prevent infections that cause cancer, such as human papillomavirus (cervical, anal and oral cancers) and hepatitis B virus (liver cancer).

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