

Vaccine, anti-PD1 drug show promise against incurable HPV-related cancers

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Electron micrograph of a negatively stained human papilloma virus (HPV) which occurs in human warts. Credit: public domain

A tumor-specific vaccine combined with an immune checkpoint inhibitor shrank tumors in one third of patients with incurable cancer related to the human papilloma virus (HPV) in a phase II clinical trial led by investigators at The University of Texas MD Anderson Cancer Center

and reported in *JAMA Oncology*.

"That encouraging response rate is about twice the rate produced by PD1 checkpoint inhibitors in previous [clinical trials](#), so these results will lead to larger, randomized clinical trials of this combination," said principal investigator Bonnie Glisson, M.D., professor of Thoracic/Head and Neck Medical Oncology and Abell-Hanger Foundation Distinguished Professor at MD Anderson.

Vaccines specific to HPV antigens found on tumors had previously sparked a strong immune response, but had not, by themselves, been active against established cancers, Glisson said.

"Vaccines are revving up the immune system, but the immunosuppressive tumor microenvironment probably prevents them from working," Glisson said. "Our thinking was that inhibition of PD-1 would address one mechanism of immunosuppression, empowering the vaccine-activated T lymphocytes to attack the [cancer](#)."

The team combined the vaccine ISA101, which targets important peptides produced by the strongly cancer-promoting HPV16 genotype of the virus, along with nivolumab, a checkpoint inhibitor that blocks activation of PD-1 on T cells.

Of the 24 patients with recurrent HPV16-related cancers, 22 had oropharyngeal (back of the throat) cancer, one had cervical cancer and one had anal cancer.

- Eight (33 percent) had a tumor response, two were complete. All eight had oropharyngeal cancer. Median duration of response was 10.3 months.
- Overall median survival was 17.5 months, progression-free survival was 2.7 months and 70 percent of patients survived to 12

months.

- Five of the eight responders remain in response.

"The median survival of 17.5 months for these patients is promising and provides further support for randomized trials testing the contribution of ISA101 to PD-1 inhibition," Glisson said.

HPV causes nearly all cervical cancers, and most oropharyngeal, anal, penile, vulvar and vaginal cancers. HPV16 and HPV18 are the leading viral genotypes that increase cancer risk. Given the viral cause of these cancers, immunotherapy has been considered a strong potential approach. The researchers note that three previous clinical trials of PD1 inhibitors alone for recurrent HPV-related cancers yielded response rates ranging from 16 to 22 percent.

Two patients had grade 3 or 4 side effects—elevated enzyme levels—that required them to discontinue nivolumab. Glisson said the team observed side effects expected from the two treatments separately, but the researchers were encouraged to see no sign of synergistic side effects caused by the combination.

"That's important as we develop rational combination immunotherapy," Glisson said. This clinical trial was among the first to combine vaccination with PD1 inhibition.

Randomized clinical [trials](#) of the vaccine and anti-PD1 combination for cervical and oropharyngeal cancer are being organized.

The single-arm trial was an investigator-initiated effort originated at MD Anderson, Glisson noted.

Provided by University of Texas M. D. Anderson Cancer Center

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