Investigational breast cancer vaccine plus immune therapy work well in tandem

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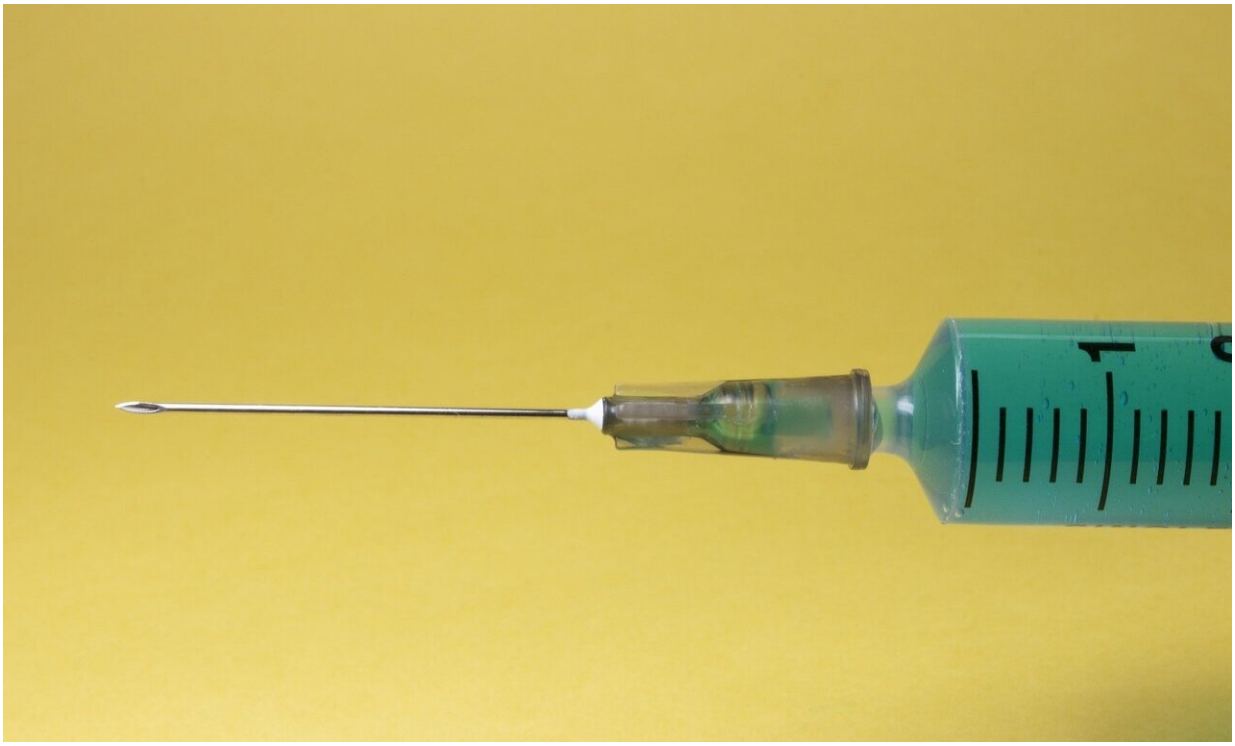

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A vaccine for HER2-positive breast cancers that is being tested in a clinical trial at Duke Cancer Institute is part of an effective, two-drug strategy for enlisting the immune system to fight tumors, according to a Duke-led study in *Clinical Cancer Research*, a journal of the American Association for Cancer Research.

The vaccine was developed at Duke and targets the HER2 protein, which is the driver of HER2-positive breast cancer and the cause of about 20 percent of all breast cancer cases.

While the vaccine works to a degree on its own, the tumor can still activate backup strategies for survival. But when combined with existing immune checkpoint inhibitors, the one-two punch proves highly effective, the researchers found.

"This study supports the development of vaccines targeting tumor driver and resistance genes, which we think is critical in establishing effective anti-tumor immune responses," said study leader Zachary Hartman, Ph.D., an assistant professor in the departments of Surgery and Pathology at Duke University School of Medicine.

Hartman and colleagues found that vaccine-induced HER2-specific T-cells were essential for immune responses. Additionally, it was more effective to elicit the T-cells early in tumor development—a finding that has implications for clinical trial designs that typically enroll patients after standard therapies have failed.

Treatment with the investigational vaccine was significantly enhanced when combined with the checkpoint inhibitor drug pembrolizumab. When used alone, pembrolizumab has shown limited benefit for HER2-positive breast cancers.

By working in tandem, the vaccine primes the immune system and the checkpoint inhibitor then rallies the T-cells to action, resulting in pronounced tumor reduction and long-term tumor-free survival.

"The basic premise is that the immune checkpoint inhibitors work fantastic if the body has already triggered an immune response, but they don't work well in the absence of that," said H. Kim Lyerly, M.D., a

professor in the departments of Surgery, Immunology and Pathology at Duke University School of Medicine and an author of this study.

"Our vaccine initiates the anti-tumor response, and in combination with the checkpoint inhibitors, works beautifully," Lyerly said.

More information: Erika J. Crosby et al. Stimulation of Oncogene-Specific Tumor-Infiltrating T Cells through Combined Vaccine and αPD-1 Enable Sustained Antitumor Responses against Established HER2 Breast Cancer. *Clinical Cancer Research* DOI: 10.1158/1078-0432.CCR-20-0389

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