Oncolytic virus treatment produces promising results in patients with triple-negative breast cancer

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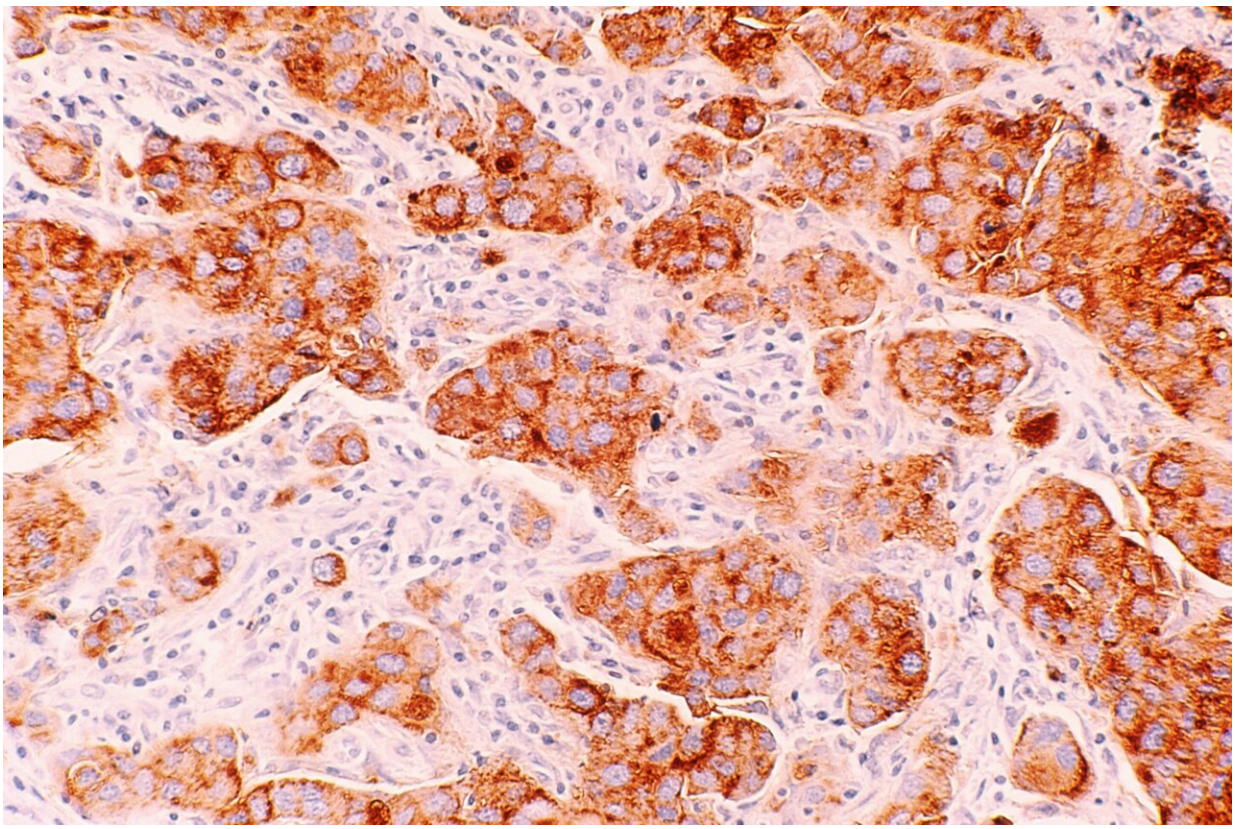

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Triple-negative breast cancer accounts for approximately 15% of all breast cancer cases. Patients with this subtype typically have poorer

outcomes compared to other breast cancers, suggesting the need for improved treatments. One new therapy being investigated at Moffitt Cancer Center involves oncolytic viruses, which infect and kill the cancer cells. In a new article published in *Nature Medicine*, the researchers, led by Hatem Soliman, M.D., share results from a phase 2 clinical trial of the oncolytic virus talimogene laherparepvec (TVEC) combined with standard chemotherapy in patients with early stage triple-negative breast cancer.

Patients with triple-negative breast cancer lack expression of the estrogen and progesterone receptors and have little to no expression of the protein HER2. As a result, hormone therapy and medicines that target HER2 protein receptors are not effective against this type of cancer. Standard therapy for early stage triple-negative breast cancer has been cytotoxic chemotherapy with the recent addition of pembrolizumab. However, this approach is associated with significant side effects. Many studies have shown that patients who have higher levels of immune cells within their tumors tend to have better responses to therapy. These observations suggest that agents that stimulate the immune system may be beneficial in triple-negative breast cancer.

TVEC is a modified herpes simplex 1 virus that includes coding sequences for the protein GM-CSF, which can stimulate the immune system. It is injected directly into the tumor and undergoes replication within the tumor cells, resulting in the breakdown of the tumor cell and production of tumor derived antigens. Immune cells can recognize the antigens, infiltrate the tumor and target the cancer cells for destruction. In addition, GM-CSF made by the virus acts as a beacon to help recruit immune cells to the tumor.

TVEC is approved to treat advanced, late stage melanoma. Moffitt researchers wanted to assess whether the oncolytic virus also could be effective in combination with standard chemotherapy when given to

triple-negative breast cancer patients before surgery. In a phase 2 trial of 37 patients, 45.9% achieved a response, 89% of the patients remained disease free two years post-treatment, and no recurrences occurred in patients who achieved strong responses. The safety profile did not differ significantly from what was expected of standard chemotherapy, except for higher levels of low grade fevers, chills, headaches and injection site pain.

The researchers also analyzed levels of immune biomarkers and assessed whether these biomarkers correlated with patient responses. They discovered that most tumor samples had higher levels of tumor fighting T cells and activation of immune signaling pathways during the first six weeks of treatment. Patients who had better responses to therapy had higher levels of CD8 T cells at week six than patients who did not respond as well to therapy. These observations suggest that activating an immune response earlier may lead to better outcomes in triple-negative breast cancer patients.

"Our results demonstrate that TVEC, when added to systemic chemotherapy, may increase responses in high risk, early stage triple-negative breast cancer. There is evidence of robust immune activation within the tumor, and additional investigation of TVEC in combination with current chemoimmunotherapy for triple-negative breast cancer is warranted," said Soliman, lead study author, medical director of Moffitt's Clinical Trials Office and senior member of Moffitt's Breast Oncology Department.

More information: Hatem Soliman, Oncolytic T-VEC virotherapy plus neoadjuvant chemotherapy in nonmetastatic triple-negative breast cancer: a phase 2 trial, *Nature Medicine* (2023). DOI: 10.1038/s41591-023-02210-0.
www.nature.com/articles/s41591-023-02210-0

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