Adoptive cell therapy plus checkpoint inhibitors show promise in non-small cell lung cancer

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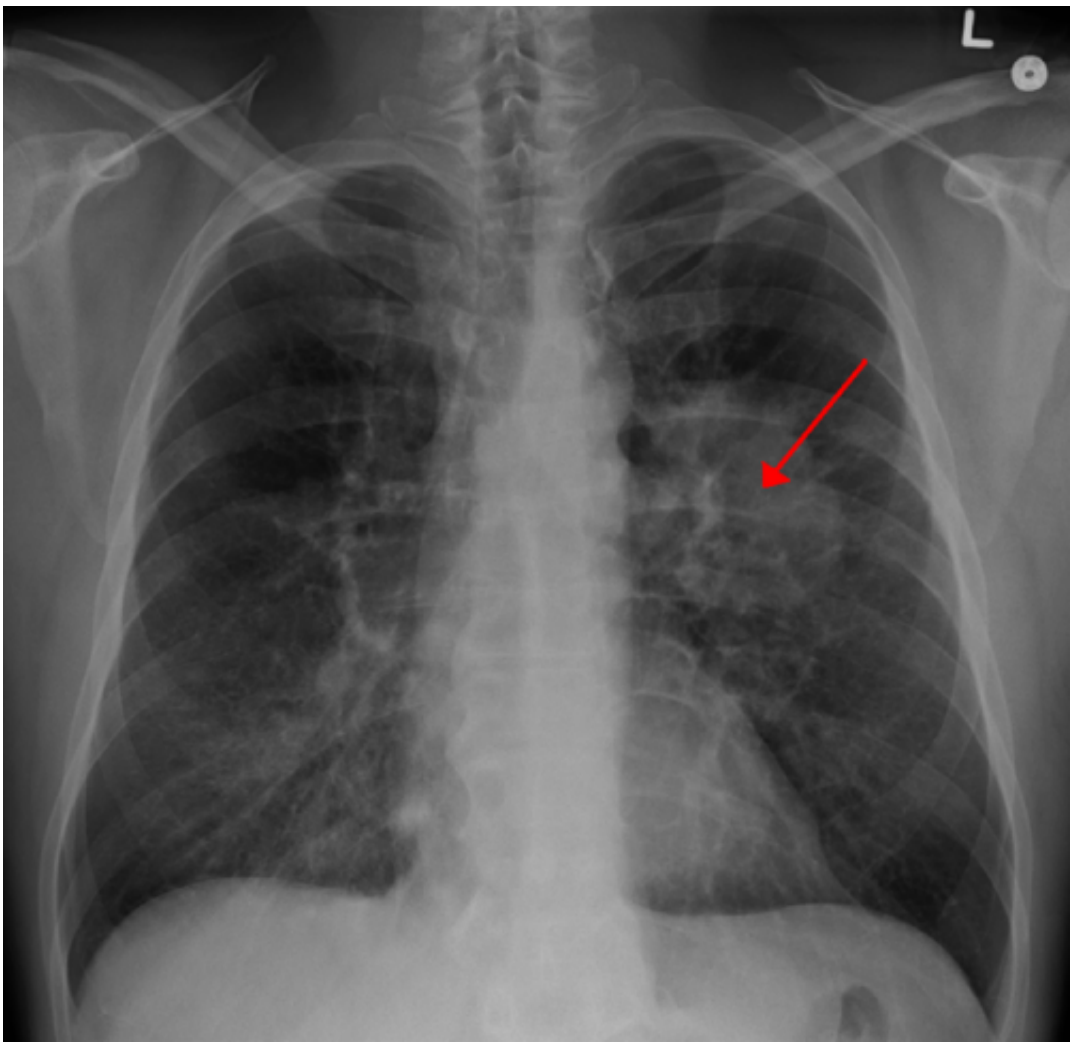

Lung CA seen on CXR. Credit: CC BY-SA 4.0 James Heilman, MD/Wikipedia

Immunotherapy has become an important tool in the treatment of lung cancer, especially checkpoint inhibitors that block certain immune checkpoints to allow immune cells to recognize and kill cancer cells. Several checkpoint inhibitors targeting PD-1 and PD-L1 have been approved for the treatment of non-small cell lung cancer. However, many patients do not respond well to this therapy creating a need for alternative treatment options.

Researchers in Moffitt Cancer Center's Lung Cancer Center of Excellence believe a combination of checkpoint inhibitors with adoptive cell therapy could be the answer for these patients. Results of their investigator-initiated phase 1 clinical trial evaluating the checkpoint inhibitor nivolumab in combination with tumor infiltrating lymphocyte (TIL) therapy were published today in *Nature Medicine*.

Non-small cell lung cancer tumors are often categorized as a "cold" tumor, meaning the tumor has not been infiltrated with immune cells making it hard to mount a response to immunotherapy.

"These results really give hope to adding cell therapy to the armamentarium for treatment of lung cancer. The TILs give the immune system a boost by providing more T cells to mount an attack, and the checkpoint inhibitor prevents the tumor from inactivating the T cells that infiltrate the tumor," said Eric Haura, M.D., associate center director of Clinical Science at Moffitt.

Twenty non-small cell lung cancer patients were enrolled in the pilot study. Each patient had one or more of their tumors removed. Those tumors were sent to the lab where each was dissected to remove the immune cells that had penetrated. These cells, called tumor infiltrating lymphocytes, were then cultured and expanded to be reinfused into the patient.

Before TIL therapy, each patient was treated with nivolumab. If the patient experienced disease progression after checkpoint inhibitory therapy, they were infused with their personalized TIL therapy followed by nivolumab maintenance therapy.

The researchers were able to successfully expand TILs for 95% of patients, and 16 out of 20 patients received the TIL infusion because their disease progressed after initial nivolumab therapy. The treatment combination resulted in promising anti-tumor activity, with 11 out of 16 patients experiencing tumor regression. Two patients had complete tumor responses that were ongoing after 18 months, and two patients had either a partial response or maintained clinical remission.

After treatment, the researchers performed additional studies and confirmed that the patients had T cells that were reactive to multiple different tumor specific proteins, including proteins with genetic mutations.

"Our data indicate that TIL can mediate effective tumor responses in subtypes that are not sensitive to traditional immune checkpoint targeted therapy. Therefore, we believe TIL may extend the scope and impact of immunotherapy into wider populations," said Ben Creelan, M.D., associate member of the Department of Thoracic Oncology at Moffitt.

A new study is being developed to improve the TIL production and expand testing in oncogene- driven lung cancer patients whose tumors progressed on targeted agents. Ongoing work from the current study is determining why some patients respond best and why some tumors progress despite initial responses from TIL.

More information: Benjamin C. Creelan et al, Tumor-infiltrating lymphocyte treatment for anti-PD-1-resistant metastatic lung cancer: a phase 1 trial, *Nature Medicine* (2021). DOI:

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