Experimental immunotherapy shows high response rate in advanced lung cancer

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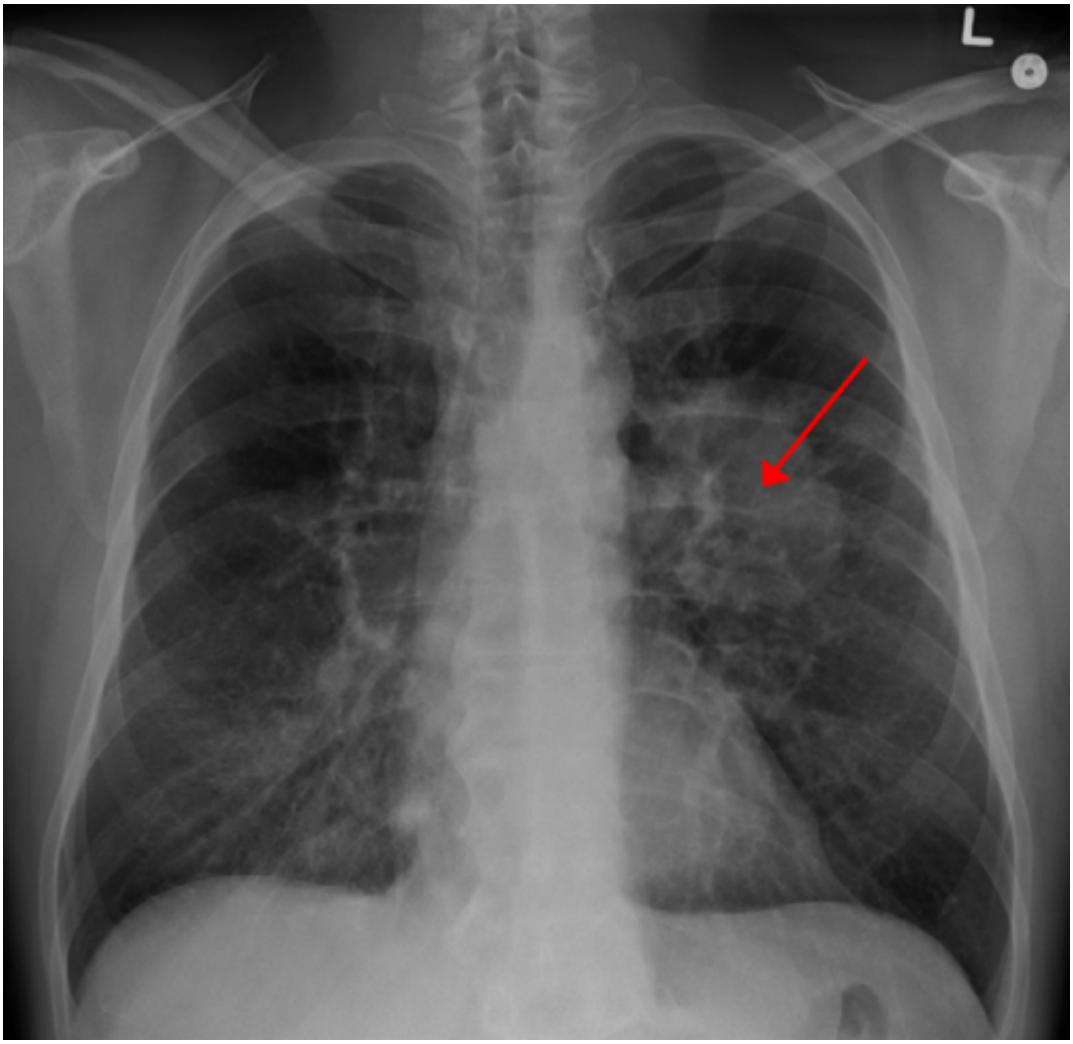

Lung CA seen on CXR. Credit: CC BY-SA 4.0 James Heilman, MD/Wikipedia

An early phase study testing an anti-PDL1 agent in combination with standard chemotherapy in the treatment of advanced non-small cell lung cancer has provided promising early results, prompting multiple phase III studies in lung cancer. The findings are being presented at the annual meeting of the American Society of Clinical Oncology (ASCO).

In this phase 1b study, patients with untreated non-small cell lung cancer received one of three standard platinum-based chemotherapy regimens (paclitaxel/carboplatin, pemetrexed/carboplatin or nab-paclitaxel/carboplatin) with MPDL3280A, an antibody targeting PD-L1. Early results from the first 37 patients showed impressive response rates between 60-75 percent, comparing favorably to historical outcomes with chemotherapy alone, where historical response rates from randomized trials are around 30 - 35 percent. In addition, two complete responses already have been documented, with no evidence of lung cancer on CT scans.

"A complete response is not typically seen in patients with stage IV lung cancer," says the abstract's lead author, Stephen V. Liu, MD, assistant professor of medicine at Georgetown Lombardi Comprehensive Cancer Center. "And the response rates seen with MPDL3280A and chemotherapy were higher than one would expect with chemotherapy alone."

Researchers say the combination therapy was well tolerated by patients, with no unexpected toxicities. The most frequently reported adverse events were linked to use of chemotherapy, investigators report, including nausea, fatigue, and constipation. Side effects associated with MPDL3280A use included anemia, low levels of neutrophils, which can increase the risk of infection, and low platelet counts, which can increase the risk of bleeding.

The research team includes researchers from University of Colorado;

Duke University Medical Center; Massachusetts General Hospital; Carolina BioOncology Institute; Dana-Farber Cancer Institute; and Yale Cancer Center.

Anti-PD-L1 and anti-PD1 antibodies are designed to enhance the activity of T-cells (immune cells), white blood cells capable of destroying cancer cells. "The body needs to tightly regulate immune function," Liu explains. "When T-cells are activated under normal conditions, they are quickly suppressed, to prevent over-activation. This suppression is controlled by the interaction of PD1 (a receptor on the immune cells) and PD-L1, the protein that binds to the PD1 receptor.

"The problem is that many tumors express PD-L1 and are able to escape T-cell immunity," Liu says. "So these drugs are designed to keep the immune signal on."

The U.S. Food and Drug Administration has approved two anti-PD1 antibodies for the treatment of refractory melanoma and one anti-PD1 antibody for the treatment of refractory squamous cell lung cancer, he says. "MPDL3280A represents an approach at targeting not PD1, but its ligand, PD-L1, which may provide some advantages. The combination with chemotherapy in the first line setting certainly deserves further study," Liu says.

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