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New immunotherapy study will pit PD-1 inhibitor against advanced lung cancer

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Penn Medicine researchers have begun a new immunotherapy trial with the "checkpoint inhibitor" known as pembrolizumab in patients with oligometastatic lung cancer—a state characterized by a few metastases in a confined area—who have completed conventional treatments and are considered free of active disease but remain at a high risk for recurrence.

The phase II trial, led by Joshua Bauml, MD, assistant professor of Hematology/Oncology in Penn's Abramson Cancer Center, is examining, for the first time, whether the immune-stimulating drug can potentially slow disease progression and potentially improve survival in non-small cell lung cancer (NSCLC) patients with oligometastatic disease, a group that fares better than more advanced lung cancer patients but is still faced with grim statistics.

Today, there is little to no data to guide clinicians treating NSCLC patients with oligometastatic disease after definitive treatment. Many of these patients benefit from chemotherapy and radiation initially, but the cancer ultimately progresses and the patients die of metastatic disease. Overall survival for patients with oligometastatic disease is 20 months, while overall survival for patients with metastatic disease is six to 12 months.

"NSCLC has historically been resistant to most immunotherapies, but PD-1 directed therapies have promise, yielding some impressive clinical responses in patients," said Bauml. "Use of the drug in this group could

be ideal since the overall burden of disease is low—they have been deemed nearly cancer-free—and the patients are generally fit and more able to tolerate the therapy. We want to find out if we may be able to utilize this 'window of opportunity' to rev up the immune system and keep metastatic cancer at bay."

Pembrolizumab (manufactured by Merck, which will fund the new trial) has received considerable attention in the last few years because of its success for the treatment of melanoma (it received FDA approval in the fall of 2014 for use in patients who have stopped responding to other treatments) and more recently, because of early results in trials for lung and other cancers.

The new ACC trial builds off previous findings in patients with NSCLC, including data from last year's American Society of Clinical Oncology annual meeting, where researchers from California reported "robust anti-tumor activity" with the drug. The response rate was 20 percent for patients on pembrolizumab.

The drug specifically blocks the programmed death receptor (PD-1) pathway known to inhibit the activation of T cells. Removing these so called immune system "brakes" with the anti-PD-1 drug has been shown to reactivate the immune system to attack tumors.

The ACC trial will enroll 42 patients with oligometastatic disease who have undergone definitive treatment to all identifiable tumor sites, which could include surgery, chemotherapy, radiation and other ablative therapies.

Four to twelve weeks after finishing their other therapies, the patients will be treated with pembrolizumab every three weeks and continue for at least six months. Primary objectives of the trial, which will last three years, include progression free survival and toxicities from the drug.

Quality of life and overall survival will also be assessed.

Provided by University of Pennsylvania