

Immunotherapy drug for advanced lung cancer shows promise

April 14 2020, by Anne Doerr



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Lung cancer spreads to the brain in about one-quarter of patients with an advanced form of the disease. To date, radiation has been the only treatment option, but it comes with toxic side effects. Researchers at

Yale Cancer Center (YCC) have found that use of the checkpoint inhibitor pembrolizumab in place of radiation can extend life with very few side effects in this patient population.

The findings, published April 13 in *The Lancet Oncology*, found that patient response depended on the level of the biomarker (PD-L1) expressed in their tumors. Of those that did respond, overall survival at one year was 40% and 34% at two years.

"Survival in this cohort of patients exceeds the historically documented survival for patients with [brain metastasis](#) from non-[small cell lung cancer](#) or NSCLC, which is a two-year survival of about 14%," said the study's lead investigator Sarah B. Goldberg, M.D., M.P.H., associate professor of medicine (medical oncology) at YCC.

This is the first study to specifically test the benefit of the treatment in a prospective clinical trial of lung cancer patients who had not yet been treated for brain metastasis or whose tumors recurred after radiation. Before this, most clinical trials of a checkpoint immunotherapy drug did not include patients with brain metastasis, but the few that did provided hints of benefit when retrospectively analyzed.

"We have clearly shown, for the first time, that brain metastasis responds to a targeted immunotherapy treatment for lung cancer," Goldberg said. "In general, we found that the benefit offered by pembrolizumab to the lungs in patients with advanced [lung cancer](#) was mirrored in control of their brain tumors. The brain and body response were the same."

This phase 2, single institution, open label study enrolled 42 patients with small brain tumors (5-20 mm) that had not been previously treated or that progressed after radiation treatment.

Patients did not have neurologic symptoms. "We did not enroll patients

with larger tumors or neurologic issues because, as the first study of this protocol, we did not know if there would be side effects and we did not want to cause harm," said Goldberg. "As it turns out, we found the drug was safe, and the neurologic adverse events were very few and unrelated to the drug."

Patients were divided into two groups: patients in cohort 1 had some PD-L1 activity; those in cohort 2 had none. Researchers found that none of the six patients in cohort 2 responded to pembrolizumab.

Goldberg theorizes that patients in cohort 1 who had a good, long-lasting response likely had brain tumors that had increased PD-L1 expression and so experienced a longer-lasting benefit. "But we don't know that yet. This idea needs to be tested."

With further study and biomarker analysis, Goldberg added, "It might make sense for some patients to try a checkpoint inhibitor first to treat both their [lung cancer](#) and brain metastasis. Radiation could follow, if necessary." But she added that such a change would take time to become a tool in the NSCLC brain metastasis medical kit. "The standard of care is radiation, and sometimes, whole [brain radiation](#). Further investigation of this therapy is needed."

More information: Sarah B Goldberg et al. Pembrolizumab for management of patients with NSCLC and brain metastases: long-term results and biomarker analysis from a non-randomised, open-label, phase 2 trial, *The Lancet Oncology* (2020). [DOI: 10.1016/S1470-2045\(20\)30111-X](#)

Provided by Yale University

Citation: Immunotherapy drug for advanced lung cancer shows promise (2020, April 14)
retrieved 2 May 2024 from

<https://medicalxpress.com/news/2020-04-immunotherapy-drug-advanced-lung-cancer.html>

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