Five-year survival rate for nivolumab-treated advanced lung cancer patients much higher than historical rate

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Treatment with the immune checkpoint inhibitor nivolumab (Opdivo) yielded durable responses in some patients with advanced non-small cell lung cancer (NSCLC), with a five-year survival rate of 16 percent, according to data from a phase I clincal trial presented here at the AACR Annual Meeting 2017, April 1-5.

According to the National Cancer Institute's SEER data, five-year survival rate for patients with advanced lung and bronchus cancer is 4.3 percent, and for those with advanced NSCLC, it is 4.9 percent.

"This is the first report of the long-term survival rate in patients with metastatic NSCLC treated with an immune checkpoint inhibitor. Our study results show that for a small subset of patients, immunotherapy can work for a very long time," said Julie Brahmer, MD, associate professor of oncology at the Bloomberg~Kimmel Institute for Cancer Immunotherapy at Johns Hopkins.

"The five-year overall survival rate reported in this study is much higher than what is reported for this population of patients receiving standard-of-care treatment. Statistics show that most patients with advanced disease die within a year of diagnosis, and the five-year survival rate for metastatic NSCLC is about 4 percent," Brahmer added.

Brahmer and colleagues used data from a cohort of the phase I clinical

trial CA209-003, in which patients with heavily pretreated, advanced NSCLC were enrolled regardless of their tumor PD-L1 status and randomly assigned to three different dose levels of nivolumab. Prior analysis of data from this trial showed nivolumab had promising clinical activity in this patient population, and data from subsequent clinical trials led to the U.S. Food and Drug Administration approving nivolumab for second-line treatment of patients with advanced NSCLC.

After following 129 patients in the phase I trial for a minimum of about 58 months, overall survival rates in patients with squamous and non-squamous NSCLC were 16 percent and 15 percent, respectively.

Of the 16 patients who survived for five years or longer, nine were male, and 12 were current smokers when they enrolled in the trial. Twelve had a partial response, and two patients each had stable disease and progressive disease as best response to treatment.

Eight patients completed the two-year treatment without any side effects, and four stopped treatment early due to side effects. None of these 12 patients required further treatment, according to Brahmer. "While this speaks to the durability of the responses, further evaluations would be needed to ascertain if the cancers were completely eliminated by the immune system, because of which no further treatment was needed, or if the therapy invoked an ongoing immune memory," Brahmer noted.

"We were unable to see a consistent pattern, a clinical or tumor characteristic, to predict which metastatic lung cancer patients are going to be five-year survivors," Brahmer noted. While baseline tumor biopsy was required for enrollment in the trial, several patients did not have adequate tumor sample to determine the PD-L1 status, she said. The presence and quantity of the protein PD-L1 is considered as a biomarker that can identify patients likely to respond to immune checkpoint

inhibitors that target the PD-1/PD-L1 pathway, such as nivolumab. However, PD-L1 status was not associated clearly with long-term survival in this small group of patients.

"We are performing further studies to learn why these patients did so well for so long and better understand which patients can stop treatment at two years and which of them need to continue treatment beyond two years," Brahmer said.

A limitation of the study is that this was not a randomized trial, hence, survival rate could only be compared with historical rates, Brahmer said.

More information: Suzanne L. Topalian et al. Safety, Activity, and Immune Correlates of Anti–PD-1 Antibody in Cancer, *New England Journal of Medicine* (2012). DOI: 10.1056/NEJMoa1200690

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