Do Smokers Respond Better to Immunotherapy for Lung Cancer?

Current and former smokers had better clinical outcomes with checkpoint inhibitors for lung cancer than nonsmokers.

August 3, 2021 By Sukanya Charuchandra

Smoking appears to improve clinical outcomes in people with non-small-cell lung cancer (NSCLC) who were treated with an immune checkpoint inhibitor, according to findings published in the Journal of the National Cancer Institute.

PD-1, a receptor on T cells that regulates immunity, can sometimes be commandeered by a tumor to turn off immune responses. Drugs that block PD-1 or its binding partner, known as PD-L1, can release the brakes and restore T-cell activity. Such drugs are known as immune checkpoint inhibitors. While immunotherapy of this kind is known to work well in some individuals, potential factors that contribute to its effectiveness are not fully understood.

David Christiani, MD, MPH, of Harvard University, and colleagues studied the potential link between smoking history and clinical outcomes of immunotherapy in people with metastatic NSCLC. They included 644 people with advanced NSCLC who were being treated with immunotherapy from April 2013 to September 2020 at the Dana-Farber Cancer Institute and Brigham and Women's Hospital, both in Boston. The team noted smoking history and clinical features, among other factors.

Some 105 (16%) of the 644 participants had never smoked, 375 (58%) had smoked a median of 28-pack years in the past and 164 (25%) were still smoking a median of 40 pack-years. A pack-year is equivalent to smoking one pack containing 20 cigarettes every day for a year.

Even after adjusting for the level of PD-L1 expression in tumors, current and former smokers had better responses to checkpoint inhibitors and longer periods of disease-free survival than individuals who had never smoked.

The researchers found that doubling the pack-year was linked to much better clinical outcomes for individuals treated with immunotherapy. Irrespective of their PD-L1 level, participants who were current or former smokers were more responsive to therapy, lived longer without their disease worsening and had better overall survival.

One possible explanation for the link may be that smoking leads to more tumor mutations, which makes cancer easier for T cells to recognize.

“Increased smoking exposure had a statistically significant association with improved clinical outcomes in metastatic NSCLC treated with [immune checkpoint inhibitor] monotherapy independent of PD-L1 [tumor proportion score],” wrote the researchers. Further, pack-years could “inform prompt clinical decisions and allow more patients to benefit from [immune checkpoint inhibitors].”

Click here to read the study in the Journal of the National Cancer Institute.
