# Combos for Lung Cancer

Immunotherapy worked better than chemotherapy as first-line treatment for people with a favorable biomarker.

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Checkpoint inhibitor immunotherapy continues to look promising for people with advanced non-small-cell lung cancer (NSCLC). Accounting for more than 80 percent of all lung cancers, NSCLC is often diagnosed at a late stage and has a high mortality rate.

Some tumors can turn off cancer-fighting T cells by hijacking the immune checkpoint PD-1, a protein that regulates immune function. Drugs that block the interaction between PD-1 on T cells and its PD-L1 binding partner on cancer cells can release the brakes and restore T-cell response. But they don't work for everyone; researchers hope that combining them with other medications can help jump-start T-cell activity.

As reported at this year's American Association for Cancer Research annual meeting in April, the KEYNOTE-189 study showed that adding Keytruda (pembrolizumab) to Alimta (pemetrexed) and platinum-based chemotherapy delayed disease progression and improved overall survival in people with previously untreated metastatic nonsquamous NSCLC, regardless of PD-L1 levels.

At the ASCO meeting, researchers reported that a different checkpoint inhibitor, Tecentriq (atezolizumab), plus the VEGF inhibitor Avastin (bevacizumab) and chemotherapy led to longer overall survival for people with advanced nonsquamous NSCLC. Soon afterward, Genentech announced results from another study showing that a combo of Tecentriq plus Alimta and platinum-based chemotherapy led to an improvement in progression-free survival in this group.

For people with PD-L1–positive tumors—that is, tumors with PD-L1 levels of 1 percent or higher—Keytruda alone might be enough. Gilberto Lopes, MD, of the University of Miami's Sylvester Comprehensive Cancer Center, reported that Keytruda monotherapy led to longer overall survival than platinum-based chemotherapy plus Alimta or paclitaxel in those with PD-L1–positive advanced NSCLC. Survival and response rates were even higher in people with PD-L1 levels above 20 percent and above 50 percent.

"A large number of patients with lung cancer now have a new treatment option with better efficacy and fewer side effects than standard chemotherapy," Lopes says.

Commenting on the study, Leena Gandhi, MD, PhD, of NYU Langone Health Perlmutter Cancer

Center in New York, noted that the benefits of Keytruda monotherapy were largely driven by people with higher PD-L1 levels. It is still not clear whether Keytruda monotherapy or the Keytruda plus chemo combo in her own KEYNOTE-189 study is a better first-line option for advanced NSCLC. In the near future, biomarkers may help doctors predict which patients will benefit from which immunotherapy regimen. “Lung cancer is no longer one size fits all,” she says.

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