Imfinzi Improves Survival for People With Advanced Lung Cancer

Immunotherapy led to better outcomes for patients with inoperable non-small-cell lung cancer.

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Treatment with Imfinzi (durvalumab) led to slower disease progression and longer overall survival for people with Stage III non-small-cell lung cancer (NSCLC) that cannot be surgically removed and has not progressed after chemotherapy and radiation, according to study results presented this week at the 19th World Conference on Lung Cancer (WCLC) in Toronto and published in The New England Journal of Medicine.

Imfinzi reduced the risk of death by 31 percent at two years. The investigators said the PACIFIC study is "the first study to demonstrate a survival advantage for unresectable Stage III NSCLC."

Non-small-cell lung cancer, which accounts for more than 80 percent of all lung cancers, is often detected late and has a high mortality rate. About 234,000 people will be diagnosed with lung cancer and about 154,000 will die from it this year, according to the American Cancer Society.

Imfinzi, from AstraZeneca, is a checkpoint inhibitor that blocks the PD-L1 protein on cancer cells. PD-1 is an immune checkpoint, a receptor on T cells that plays a role in regulating immune function. Some tumors can hijack PD-1 to turn off immune responses against them. Drugs that block the interaction between PD-1 and its binding partner PD-L1 can release the brakes and restore T-cell activity. Recent research shows that chemotherapy and radiation lead to tumor inflammation that attracts T cells, which may help checkpoint immunotherapy work better.

Scott Antonia, MD, PhD, of Moffitt Cancer Center and Research Institute in Tampa presented follow-up findings from PACIFIC, an international Phase III clinical trial that enrolled 713 patients with Stage III NSCLC.

Stage III lung cancer has spread beyond the lungs to nearby lymph nodes or structures in the chest but not yet to distant parts of the body. About a third of people newly diagnosed with NSCLC have Stage III disease. It is usually unresectable, meaning it cannot be completely removed by surgery. Standard treatment involves platinum-based chemotherapy and radiation therapy, but in most cases, the cancer eventually progresses and the five-year survival rate using this approach is as low as 15 percent, according to Antonia.

PACIFIC participants had not yet experienced disease progression following chemotherapy and radiation. A majority (70 percent) were men, 69 percent were white and 27 percent were Asian. About 40 percent had PD-L1 levels below 25 percent, 22 percent had higher levels and 37 percent had not been tested. Higher PD-L1 levels are associated with better response to checkpoint inhibitors but do not reliably predict response in individual patients.

Within one to 42 days after completing chemotherapy and radiation, study participants were randomly assigned to receive Imfinzi or placebo by IV infusion once every two weeks for up to a year.

Last year the PACIFIC investigators reported that Imfinzi was associated with improved progression-free survival (PFS), meaning patients were still alive without worsening of disease. This led the Food and Drug Administration to grant Imfinzi accelerated approval for this indication this past February.

Follow-up data showed progression-free survival rates of 49.5 percent in the Imfinzi group and 26.7 percent in the placebo group at 18 months. The median PFS time was 17.2 months versus 5.6 months, respectively. People taking Imfinzi were less likely to develop new tumors in their lungs, lymph nodes, brain, liver or bones.

With longer follow-up, Imfinzi led to improved overall survival as well, Antonia reported. Two-year overall survival rates were 66.3 percent in the Imfinzi group versus 55.6 percent in the placebo group, representing a 31 percent reduction in the risk of death. The median overall survival was 28.7 months in the placebo arm but was not reached in the Imfinzi arm because a majority of patients were still alive. These differences were statistically significant, meaning they were probably not attributable to chance alone. Improvement in progression-free and overall survival was seen across PD-L1 levels.

Treatment was generally safe; 30.5 percent of Imfinzi recipients and 26.1 percent of placebo recipients experienced severe adverse events, and 15.4 percent and 9.8 percent, respectively, stopped treatment for this reason. Severe pneumonitis, or lung inflammation, developed in 3.6 percent of Imfinzi recipients and 3.0 percent of placebo recipients.

“Results of PACIFIC provide compelling evidence for the unprecedented benefit of durvalumab treatment as the standard of care in this patient population,” Antonia said in a WCLC press release. "Durvalumab offers the first major advance in this disease setting in many years, offering new hope to patients with Stage III unresectable NSCLC without progression after chemoradiotherapy.”

Click here for the World Conference on Lung Cancer program.

Click here to read the report in the New England Journal of Medicine.
