Immunotherapy Combo Improves Small-Cell Lung Cancer Survival

Imfinzi plus chemotherapy led to a modest but significant improvement in overall survival.

September 30, 2021 By Liz Highleyman

The checkpoint inhibitor Imfinzi (durvalumab) in combination with platinum chemotherapy improved overall survival for people with extensive-stage small-cell lung cancer (SCLC), according to three-year follow-up data presented at the European Society for Medical Oncology (ESMO) Congress.

Although combination treatment extended survival by just two months compared with chemotherapy alone, about three times as many patients were still alive at three years in the combination group, reported Luis Paz-Ares, MD, of Hospital Universitario 12 de Octubre in Madrid. This is the longest survival follow-up ever reported for immunotherapy for this difficult-to-treat cancer, according to AstraZeneca.

Small-cell lung cancer, which accounts for nearly 15% of all lung cancers diagnosed in the United States, is an aggressive malignancy that can progress rapidly. Because it is harder to treat and recurrence is common, the five-year survival rate for SCLC is only 7%, compared with 25% for the more common non-small-cell lung cancer, according to the American Society of Clinical Oncology.

The international Phase III CASPAIN trial (ClinicalTrials.gov NCT03043872) included 805 people with extensive-stage SCLC—metastatic cancer that has spread to the opposite lung or elsewhere in the body—who were starting treatment for the first time.

The participants were randomly assigned to receive Imfinzi with chemotherapy (etoposide plus either carboplatin or cisplatin); Imfinzi, chemotherapy and tremelimumab (a second checkpoint inhibitor); or chemotherapy alone.

Imfinzi is a monoclonal antibody that blocks the tumor protein PD-L1. PD-1 is a checkpoint protein on T cells that regulates immune function. Some cancers can hijack PD-1 to turn off immune response. Drugs that block the interaction between PD-1 and PD-L1, its binding partner, can release the brakes and restore T-cell activity. The Food and Drug Administration (FDA) approved Imfinzi for extensive-stage SCLC in March 2020. Tremelimumab, which is not yet FDA-approved, is a CTLA-4 checkpoint inhibitor that suppresses T-cell multiplication.

As previously reported at the 2019 World Conference on Lung Cancer and in The Lancet, the trial met its primary endpoint in an interim analysis, showing that adding Imfinzi to chemotherapy improved survival. After about a year and a half of follow-up, the median overall survival time was 13.0 months in the Imfinzi plus chemotherapy group versus 10.3 months in the chemotherapy-only group—a 27% reduction in the risk of death. Adding tremelimumab did not significantly increase survival.

At the ESMO meeting, Paz-Ares reported extended follow-up results after more than three years. The updated median overall survival time was 12.9 months in the Imfinzi plus chemotherapy group versus 10.5 months in the chemotherapy-only group, a 29% reduction in mortality.

But the improvement in the likelihood of survival was more impressive. In the interim analysis, 53% of patients taking the Imfinzi combination were still alive after a year, compared with 40% in the chemotherapy-only group. The corresponding figures were 34% and 25%, respectively, at 18 months, 23% versus 14% at two years, and 18% versus 6% at three years.

Treatment was generally safe, and Imfinzi did not increase side effects. Serious adverse events occurred in about a third of patients in both the Imfinzi plus chemotherapy and chemotherapy-only groups, rising to nearly half in the group that also added tremelimumab. The likelihood of adverse events leading to death was also similar in the first two groups (5% versus 6%).

“Patients with extensive-stage small cell lung cancer historically have had limited treatment options and still face a dire prognosis, which makes these data showing that three times as many patients survive three years following Imfinzi treatment especially meaningful,” Paz-Ares said in an AstraZeneca press release. “These results reinforce Imfinzi plus platinum chemotherapy as an important standard of care in this setting.”

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