Lurbinectedin Yields Favorable Outcomes in Those With Small-Cell Lung Cancer

A Phase II trial reached its primary endpoint of overall response in just over a third of participants.

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PharmaMar's lurbinectedin led to complete or partial tumor regression in more than a third of study participants with small-cell lung cancer (SCLC) who had received at least one prior treatment for the disease.

The lead author of the study, Luis Paz-Ares, MD, PhD, the head of the oncology department at the Hospital Universitario 12 de Octubre in Madrid, presented the findings at the American Society of Clinical Oncology (ASCO) annual meeting in Chicago last week.

"Lurbinectedin is showing to be a new potential treatment alternative for second-line small-cell lung cancer, where, until now, no progress has been made for more than two decades," Paz-Ares said in a press release.

Accounting for 10% to 15% of all lung cancer cases, SCLC has been less extensively studied and has fewer treatment options than the more common non-small-cell lung cancer. SCLC is often aggressive and has a high mortality rate.

Lurbinectedin is an RNA polymerase II inhibitor. It blocks transcription factors that trigger the growth of cancer, damages cancer cell DNA and suppresses the production of cytokines, or chemical messengers that promote tumor growth.

The safety and efficacy of lurbinectedin were assessed in a multicenter, single-arm Phase II basket trial that enrolled individuals with an array of solid tumors. Paz-Ares presented findings from an analysis of 105 people with SCLC who enrolled between October 2015 and October 2018. This cohort had a median age of 60 years old; 35.2% of the cohort was 65 years old or older. They had received a median of one previous treatment for SCLC.

The participants were treated with lurbinectedin at a dose of 3.2 milligrams per square meter of

height administered via an intravenous infusion (which lasted an hour) every three weeks. They received a median of four cycles of treatment. Eleven participants were still on treatment at the end of the new report's follow-up period, while 25 individuals had stopped the treatment, 66 had died and three were lost to follow-up.

During a follow-up period of 17.1 months, lurbinectedin achieved its primary endpoint, with an overall response rate of 35.2%. All 37 of the participants who fell into this category experienced a partial treatment response. Of the eight people whose previous immunotherapy failed, five (67.5%) experienced tumor shrinkage. Additionally, 35 people (33.3%) had stable disease. Together, the outcomes in these two groups yielded a disease control rate of 68.6%. Disease progressed in 28 participants (26.7%). The median duration of response was 5.3 months.

Among those with sensitive disease—meaning those who experienced a relapse after 90 days or more—the overall response rate was 45%. Among those with resistant disease—they experienced a relapse in less than 90 days—the overall response rate was 22.2%. The median duration of response was 6.2 months for sensitive patients and 4.7 months for resistant patients. There is currently no approved treatment for people with resistant SCLC.

The median overall survival for the whole cohort was 9.3 months. Median overall survival was 11.9 months for those with sensitive disease and 5.0 months for those with resistant disease.

The median progression-free survival, meaning participants were still living and did not experience worsening of their disease, was 3.9 months in the overall cohort, 4.6 months among those with sensitive disease and 2.6 months among those with resistant disease.

The most common treatment-related adverse events were fatigue, nausea or vomiting, and decreased appetite, mostly mild or moderate. A total of 22.9% of participants experienced severe (grade 3 or 4) neutropenia (low neutrophils, a type of white blood cell), 4.8% experienced severe febrile neutropenia (neutropenia plus a fever), 6.7% experienced severe anemia and 4.8% experienced severe thrombocytopenia (low platelets). Only two participants discontinued treatment because of drug-related adverse events.

The study's findings compare favorably to the data that is included in the Food and Drug Administration label for Hycamtin (topotecan), which was approved in 1996 and is the most recent drug for second-line treatment of SCLC to hit the market. In a study of Hycamtin, the overall response rate was 24%, the median progression-free survival was 3.9 months and the median overall survival was 5.8 months. However, in that study, 70% of participants experienced severe neutropenia, 28% experienced severe febrile neutropenia and 42% experienced severe anemia.

This comparison, while not conducted in a head-to-head trial, suggests that lurbinectedin shows promise as a new alternative treatment for second-line SCLC.

To read the conference abstract, click here.

To read a press release about the study, click here.
