Lurbinectedin does not improve overall SCLC survival; some positive action with doxorubicin after chemotherapy

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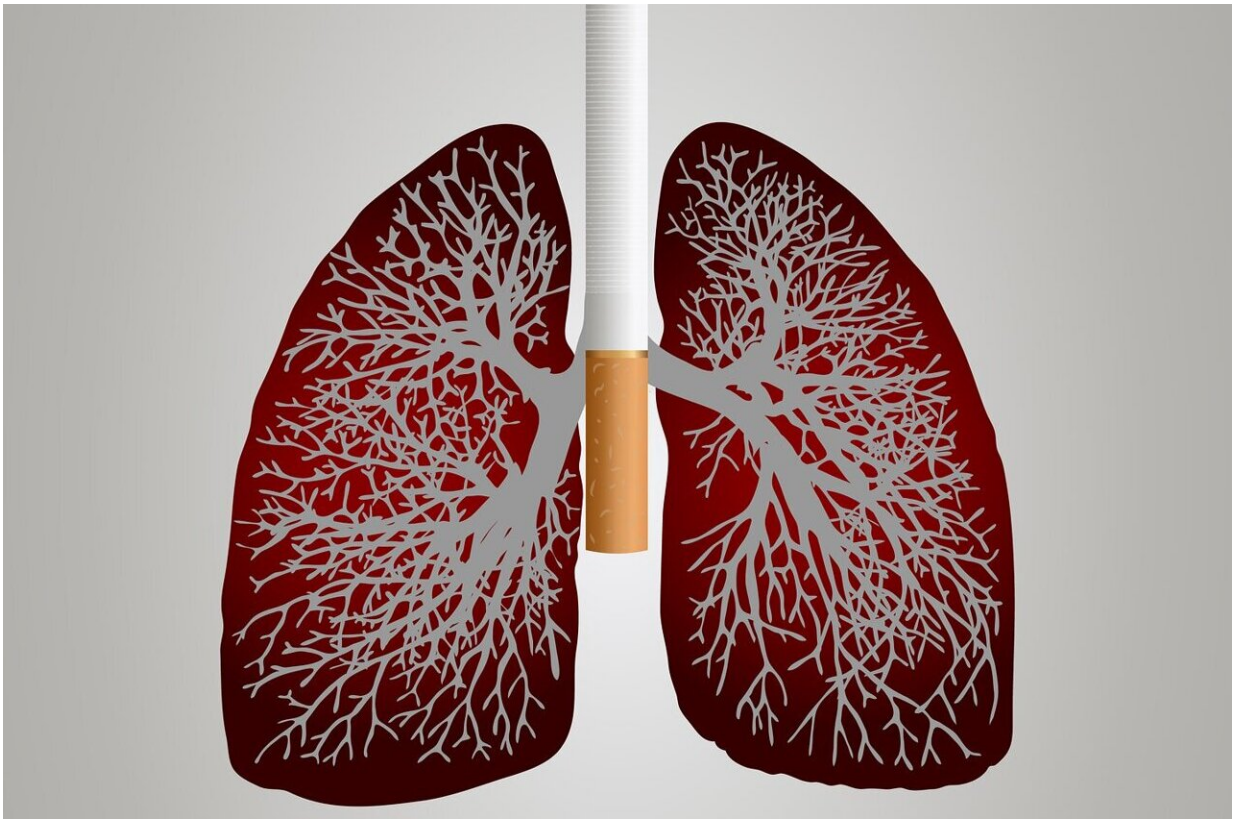

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A multicenter clinical trial with 631 patients with small cell lung cancer (SCLC) that tested the use of lurbinectedin did not meet its primary end

point of overall survival but did show that the combination of lurbinectedin and doxorubicin was active in patients with SCLC after use of one prior platinum-based chemotherapy.

The research was presented today at the IASLC 2021 World Conference on Lung Cancer meeting.

Small cell lung cancer occurs in approximately 200,000 people and there are few approved effective therapies. However, in June 2020, the U.S. Food and Drug Administration granted accelerated approval to lurbinectedin (3.2 mg/m^2 every 3 weeks) for the treatment of adult patients with metastatic SCLC who had disease progression on or after platinum-based chemotherapy.

Lurbinectedin is a novel anticancer agent that inhibits transactivated transcription and modulates tumor microenvironment. Lurbinectedin showed high activity for patients with second-line SCLC when treated in combination with doxorubicin (Ann Oncol. 2017;28(10):2559-2566; Invest New Drugs. 2021; March 11), consistent with the synergistic effects found in vitro/in vivo.

Dr. Luis Paz-Ares, of the Hospital Universitario, Universidad Complutense and Ciberonc, in Madrid, Spain, and colleagues from 17 clinical sites in Europe and the United States enrolled 613 patients. To be eligible for the trial, patients required an ECOG performance status (PS) score of 2 or less and a confirmed diagnosis of limited- or extensive-stage SCLC. Patients must have received one prior platinum-based chemotherapy course and a chemotherapy-free interval (CTFI) greater than 30 days was not effective. If CTFI was less than 30 days, the patient was not eligible.

The experimental arm administered 2 mg/m^2 of lurbinectedin plus 40 mg/m^2 of doxorubicin on day 1 every 3 weeks to patients. The control

arm administered investigator's choice of either 1,000 mg/m^2 of cyclophosphamide, 45 mg/m^2 of doxorubicin and 2 mg of vincristine (CAV) on day 1 every 3 weeks, or 1.5 mg/m^2 topotecan days 1-5 every 3 weeks. All patients were randomly assigned 1:1 and received treatment until disease progression or unacceptable toxicity.

All patients received primary prophylaxis with granulocyte colony stimulating factor (G-CSF). Stratification was performed according to the CTFI duration after first line, ECOG PS, central nervous system involvement, receipt of prior immunotherapy, and Investigator's preference for the control arm.

Median overall survival was 8.6 months (95% CI) in the experimental arm and 7.6 months in the control arm. Median progression-free survival was 4.0 months in both the experimental and control arms (95% CI). Objective response rate was higher in the experimental arm compared to the control group (31.6% vs 29.7%, respectively) and duration of response was 5.7 months in the experimental arm and 3.8 months in the control arm.

Treatment-related adverse events (AEs) were reported in 268/303 patients (88.4%) in the experimental arm and 266/289 (92.0%) in the control arm. AEs of grade 3 or greater were observed in 200 (66.0%) vs. 250 (86.5%) patients, respectively. The experimental arm showed favorable safety and tolerability with significantly lower hematologic toxicity and resulted in fewer dose reductions, treatment discontinuations, and deaths due to AEs compared to the control arm. "Although the primary objective of this study was not met, the combination of lurbinectedin and doxorubicin was active in patients with SCLC after failure of one prior platinum-containing line, especially in those with sensitive disease (CTFI ≥ 90 days) and without central nervous system involvement at baseline," reported Dr. Paz Ares. "New combinations with other cytotoxic agents such as irinotecan and immune-

check inhibitors are being explored."

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