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## ARTICLES

# Cisplatin- Versus Carboplatin-Based Chemotherapy in First-Line Treatment of Advanced Non–Small-Cell Lung Cancer: An Individual Patient Data Meta-analysis

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**Background:** Because the efficacy of carboplatin and cisplatin in the treatment of advanced non–small-cell lung cancer (NSCLC) has not been proven to be equivalent, an individual patient data meta-analysis comparing the two treatments was performed.

**Methods:** Randomized trials comparing carboplatin to cisplatin in first-line treatment of advanced NSCLC were identified and their electronic databases obtained. A general variance-based method was used to estimate the summary hazard ratios (HRs), odds ratios (ORs), and their 95% confidence intervals (CIs) for mortality, objective response, and toxicity. Cochran's chi-square test ( $Q$  test) was used to test for heterogeneity among trials, and the  $I^2$  index, which expresses the proportion of variability of the results due to heterogeneity, was calculated. A random-effects model that takes into account interstudy variation was also applied. All statistical tests were two-sided.

**Results:** Nine trials that included a total of 2968 patients were analyzed; overall median follow-up was 1021 days. The objective response rate was higher for patients treated with cisplatin than for patients treated with carboplatin (30% versus 24%, respectively; OR = 1.37; 95% CI = 1.16 to 1.61;  $P < .001$ ). Carboplatin treatment was associated with a non–statistically significant increase in the hazard of mortality relative to treatment with cisplatin (HR = 1.07; 95% CI = 0.99 to 1.15;  $P = .100$ ). In patients with nonsquamous tumors and those treated with third-generation chemotherapy, carboplatin-based chemotherapy was associated with a statistically significant increase in mortality (HR = 1.12; 95% CI = 1.01 to 1.23 and HR = 1.11; 95% CI = 1.01 to 1.21, respectively). Cisplatin-based chemotherapy was

associated with more severe nausea and vomiting and nephrotoxicity; severe thrombocytopenia was more frequent during carboplatin-based chemotherapy.

**Conclusions:** Our individual patient data meta-analysis suggests that cisplatin-based chemotherapy is slightly superior to carboplatin-based chemotherapy in terms of response rate and, in certain subgroups, in prolonging survival without being associated with an increase in severe toxic effects. Therefore, cisplatin-based third-generation regimens should remain the standard reference for the treatment of selected patients with advanced-stage NSCLC and of those with earlier-stage disease.

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## **Context and Caveats**

### **Prior knowledge**

Platinum-based chemotherapy leads to a small but statistically significant improvement in survival in patients with advanced non-small-cell lung cancer. Carboplatin had largely replaced cisplatin as the platinum-containing drug used to treat this disease because it was associated with a lower incidence of serious side effects. However, it was unclear whether the two drugs had similar clinical efficacy in the treatment of non-small-cell lung cancer.

### **Study design**

A meta-analysis of individual patient data from randomized controlled clinical trials that compared chemotherapy regimens containing either cisplatin or carboplatin.

### **Contribution**

This study presented evidence that cisplatin was more effective than carboplatin in patients treated with newer chemotherapy regimens and in patients with nonsquamous tumors. The side effects associated with the two drugs in non-small-cell lung cancer patients were clarified.

### **Limitations**

The conclusions are based on a somewhat heterogeneous group of clinical trials, some of which were small.

### **Implications**

Cisplatin may well be preferable to carboplatin in non-small-cell lung cancer patients whose disease is at an early stage and in those patients who have advanced disease with a relatively good prognosis.

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