Cisplatin/Etoposide vs Paclitaxel/Cisplatin/G-CSF vs Paclitaxel/Cisplatin in Non-Small-Cell Lung Cancer

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A phase III trial conducted by Eastern Cooperative Oncology Group (ECOG) investigators assessed the possible impact of paclitaxel on survival, response, and toxicity in patients with advanced non-small-cell lung cancer (NSCLC).

**Introduction**

In the late 1980s, Eastern Cooperative Oncology Group (ECOG) investigators conducted a series of phase III trials to evaluate a variety of combination chemotherapy regimens in patients with non-small-cell lung cancer (NSCLC). The results showed that cisplatin (Platinol)-containing regimens produced a response rate of approximately 25%, a median survival duration of six months, and a one-year survival rate of 19%. None of the regimens was associated with superior survival compared with any other regimen.

At about the same time, a series of single-agent phase II trials showed that paclitaxel (Taxol) produced a 21% response rate and a 40% one-year survival rate in patients with NSCLC. Investigators at the M. D. Anderson Cancer Center in Houston observed similar results with paclitaxel. Based on these observations, ECOG investigators initiated a phase III trial to evaluate the potential impact of paclitaxel on survival in patients with advanced NSCLC.

**Materials and Methods**

Eligibility requirements for this trial included histologic/cytologic confirmation of NSCLC: stage IIIB/IV disease without brain metastasis; ECOG performance status of 1 or less; measurable or evaluable disease; adequate bone marrow, renal, hepatic, and cardiac function; no evidence of uncontrolled hyperglycemia; no previous chemotherapy; and written informed consent.

Patients were randomly assigned to one of three regimens:

- The first consisted of cisplatin, 75 mg/m² intravenously (IV) on day one, plus etoposide (VePesid), 100 mg/m² IV on days one, two, and three.
- In the second regimen, paclitaxel, 250 mg/m² IV over 24 hours was followed by cisplatin, 75 mg/m² on day two, plus oral granulocyte colony-stimulating factor (G-CSF), 5 µg/kg starting on day three and continuing until the granulocyte count was greater than 10,000/cells/mm³.
- The third consisted of paclitaxel, 135 mg/m² IV over 24 hours, followed by cisplatin, 75 mg/m² IV on day two.

Each regimen was repeated every 21 days. The major objectives of this trial were to compare survival, response, and toxicity among the three regimens.

**Results**

Between August 1993 and December 1994, 600 patients were entered into this trial. The number of eligible patients treated with each regimen was 194 with cisplatin/etoposide, 190 with paclitaxel/cisplatin/G-CSF, and 187 with paclitaxel/cisplatin. Comparison of patient characteristics revealed no significant differences between the treatment groups. Median age was 61 years. Slightly more than one-third were women, one-third were asymptomatic, and 25% had not lost more than 5% of their usual body weight. In addition, 19% had stage IIIB disease, and 81% had stage IV NSCLC. Grade 4 granulocytopenia occurred in the majority of patients, but the incidence of deaths that were possibly related to treatment was similar to results from previous ECOG NSCLC trials: 2% for cisplatin/etoposide, 4.4% paclitaxel/cisplatin, and 5.3% for paclitaxel/cisplatin/G-CSF.

Response rates were 12% in the cisplatin/etoposide group, 31% in the paclitaxel/cisplatin/G-CSF
group, and 26% in the paclitaxel/cisplatin group. Comparison of responses using Fisher's exact test revealed significant differences between the cisplatin/etoposide and paclitaxel/cisplatin/G-CSF groups ($P < .001$) and between the cisplatin/etoposide and paclitaxel/cisplatin groups ($P < .001$); there was no significant difference in response for patients treated with paclitaxel/cisplatin vs paclitaxel/cisplatin/G-CSF ($P = .308$).

Preliminary survival analysis revealed a trend toward longer survival in patients treated with the paclitaxel regimens.

**Conclusions**

Both paclitaxel regimens were associated with significantly higher response rates compared with etoposide/cisplatin, and preliminary survival analyses suggest that the paclitaxel regimens may also be associated with superior survival.

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