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 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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