

# Carboplatin-Pemetrexed Adjuvant Chemotherapy in Resected Non-small Cell Lung Cancer (NSCLC): A Phase II Study

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**Abstract.** *Background:* The aim of this study was to determine the progression-free survival (PFS) and toxicity associated with adjuvant administration of carboplatin and pemetrexed for completely resected patients with stage IB, II and IIIA non-small cell lung cancer (NSCLC). *Patients and Methods:* Forty-five eligible NSCLC patients received surgical resection for pathological stage IB, II or IIIA followed by postoperative adjuvant chemotherapy with carboplatin AUC5 and pemetrexed administered on days 1 and 14 on a 28-day cycle. Recombinant human granulocyte colony-stimulating factor (rhG-CSF) was given prophylactically. *Results:* The mean time to disease progression of patients was 26 months. Toxicities were generally mild to moderate and entirely manageable. *Conclusion:* The administration of carboplatin and pemetrexed is a safe, well-tolerated and convenient regimen in the adjuvant setting of completely resected NSCLC, with efficacy similar to that reported in other regimens but less toxicity.

Although complete surgical resection is the optimal management of patients with operable non-small cell lung cancer (NSCLC), the five-year overall survival rate is poor, ranging from 23% to 67%, and dependent on the size of the primary tumor and the lymph node involvement (1). Postoperative radiotherapy reduces the rate of local recurrence in stage IIIA disease but it has a questionable, if not detrimental, effect in patients with stage I and II (2).

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Treatment failure following complete resection for early stage NSCLC is mainly due to the development of distant metastasis rather than local recurrence (1). The 1995 meta-analysis published by the Non-Small Cell Lung Cancer Collaborative Group suggested an absolute survival advantage at 5 years of 5% with cisplatin-based chemotherapy (3). Following this meta-analysis, three large adjuvant studies using cisplatin-based two-drug regimens for completely resected NSCLC showed absolute 5-year survival differences ranging from 4% to 15% (hazard ratio, HR: 0.69 to 0.86) (4-6). The Lung Adjuvant Cisplatin Evaluation (LACE) meta-analysis using the data from 4,584 patients in five randomized adjuvant cisplatin-based chemotherapy trials with a median follow-up of 5.2 years showed an absolute 5-year survival benefit of 5.4% (7). Although the role of cisplatin-based adjuvant chemotherapy for stage II and IIIA NSCLC is well established, there is still some uncertainty regarding its utility in stage IB. Trying to answer this question, the Cancer and Leukemia Group B (CALGB) conducted a randomized trial (CALGB 9633) in 344 stage IB NSCLC patients using a paclitaxel/carboplatin regimen. The results of this study advocated the use of adjuvant paclitaxel/carboplatin only for stage IB patients with large tumors (8). There is strong evidence for administering cisplatin-based adjuvant chemotherapy in NSCLC patients after a complete surgical resection but the difficulty is that many patients are not able to receive such therapy because of co-morbidities. The aim of this study was to test an alternative adjuvant regimen using carboplatin and pemetrexed in patients with completed resected NSCLC in order to identify the possible best outcome with the least toxicity.

## Patients and Methods

*Eligibility criteria.* Forty-five patients with a mean age of 61.2 years (40-76) and completely resected stage IB, II and IIIA NSCLC by lobectomy, bilobectomy or pneumonectomy were included in the study. Additional eligibility criteria included: age  $\geq$  18 years, Eastern Cooperative Oncology Group (ECOG) performance status  $\leq$  2,