Efficacy of adjuvant or neoadjuvant chemotherapy with surgical resection of stage IB-IIIA NSCLC

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Background: The therapeutic efficacy of adjuvant or neoadjuvant chemotherapy with surgical resection of stage IB-IIIA NSCLC has been less clear. We performed a retrospective study of adjuvant or neoadjuvant chemotherapy with vinorelbine plus cisplatin or etoposide plus cisplatin to validate the efficacy on the patients with early stage NSCLC. Response, survival data and the feasibility of chemotherapy were analyzed.

Methods: 48 patients diagnosed as stage IB-IIIA NSCLC from January 1994 to February 2006, were enrolled for analysis. All patients received either 30 mg/m² vinorelbine plus 100 mg/m² cisplatin (n=17) or 100 mg/m² etoposide plus 100 mg/m² cisplatin (n=31) every 3 weeks, before operation or after operation. In neoadjuvant setting, after 3 cycles of chemotherapy, restaging was done with chest CT, followed by surgery. Postoperative radiotherapy was at the investigator’s discretion.

Results: 10 patients (20.8%) had stage IB disease and 38 patients (79.2%) had stage IIIB disease. The adjuvant chemotherapy group was 22 (45.8%) patients and neoadjuvant chemotherapy group was 26 (54.2%) patients. The median duration of follow-up was 45.5 (6-187) months. The median survival was 46 (6-187) months and disease-free survival was 31 (5-187) months. The overall survival of patients who adjuvant chemotherapy was similar compared with the patients who neoadjuvant chemotherapy (46 vs 46 months, p=0.125). The Grade 3/4 hematologic toxicities of chemotherapy were neutropenia (n=9), anemia (n=1), and thrombocytopenia (n=1).

Conclusion: The adjuvant or neoadjuvant chemotherapy of vinorelbine plus cisplatin or etoposide plus cisplatin has an acceptable level of toxicity and may prolong overall survival among patients with completely resected stage IB-IIIA NSCLC.

Weekly Low-dose Docetaxel for Pretreated Elderly or Less Fit Patients with Non-Small Cell Lung Cancer

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Background: Second-line single-agent docetaxel showed superiority in overall survival compared with best supportive care alone in previously treated patients with non-small cell lung cancer (NSCLC). However, for elderly or less fit patients, chemotherapy is associated with greater toxicity and less benefit, and the efficacy of salvage docetaxel chemotherapy for these patients is still controversial. Therefore, we evaluated the efficacy and toxicity profiles of weekly low-dose docetaxel regimen administered in daily clinical practice for elderly or less fit NSCLC patients previously exposed to chemotherapy.

Methods: Between May 2004 and January 2007, forty unselected, consecutive and prospectively enrolled patients with stage IIIB or IV NSCLC, previously treated with one or more chemotherapy regimens, received docetaxel as single-agent salvage chemotherapy at Seoul National University Bundang Hospital. All patients were aged ≥ 65 years, or had an ECOG performance status of ≥ grade 2 in the cases of ages < 65 years. Docetaxel was administered at a dose of 25 mg/m² weekly on days 1, 8, and 15 of a 28-day cycle in an outpatient setting.

Results: Median age was 66 years (range 38 to 80). Twenty-nine patients (73%) received docetaxel as second-line chemotherapy and eleven (28%) as third- or fourth-line treatments. Platinum, gemcitabine, paclitaxel, epidermal growth factor (EGFR) inhibitors were previously employed in 39 (98%), 37 (93%), 9 (23%) and 9 patients (23%), respectively. A median of 2 cycles (range 1 to 6) were administered and, of 40 patients enrolled, nine patients (23%) showed partial responses. Nine patients (23%) showed stable disease and 17 (43%) progressive disease. Five patients (13%) were not evaluable. Grade 3/4 toxicities were rare: asthenia in 8% of patients, anorexia in 8%, mucositis in 5%, diarrhea in 3%, neutropenia in 3%, nail change in 3%, and peripheral neuropathy in 3%. Drug toxicity was the reason for the treatment discontinuation in 5 patients (13%). At median follow-up of 18 weeks, 22 patients are alive. Median progression-free survival and overall survival were 9.9 weeks (95% confidence interval [CI]: 7.1~12.7 weeks) and 37.7 weeks (95% CI: 21.0~54.3 weeks), respectively.

Conclusions: Weekly low-dose docetaxel appears to be well tolerated as salvage chemotherapy for previously treated elderly or less fit patients with NSCLC. The efficacy of this low-dose regimen seems to be comparable to the standard 3-week or higher-dose weekly docetaxel regimens. This approach provides a reasonable alternative for pretreated elderly or less fit patients with NSCLC.
Results: There was no significant difference between clinical treatment response and sex, pathological type, specimen origin, or m-P53 status in cultured cell supernatant. Telomerase activity and apoptosis rate was response and sex, pathological type, specimen origin, or m-P53 status.

The senescence of tumor cells defined as that, apoptosis rate increased more than 50% to control, and telomerase activity decreased less than 50% to control. 

Conclusions: Weekly paclitaxel with gemcitabine is effective and well tolerated as first-line treatment for advanced NSCLC patients. Long survival may be due to platinum doublet second-line chemotherapy.

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Gemcitabine and Oxaliplatin as second and third line therapy of advanced and metastatic non-small cell lung cancer (NSCLC): evidence of clinical activity and improvement in quality of life.

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Background: Gemcitabine is active as second line therapy in NSCLC. Oxaliplatin may be non-cross resistant with other platinum agents used as first-line therapy in NSCLC. The combination of gemcitabine and oxaliplatin (GEMOX) is synergistic in pre-clinical models and clinical trials have shown that it is safe and efficacious in several tumor types, including NSCLC.

Methods: A phase II trial was designed to assess the efficacy and tolerability of gemcitabine 1,000 mg/m2 over 100 min in combination with oxaliplatin 100 mg/m2 over 2 hours both given on days 1 and 15 of a 28-day cycle. Patients with NSCLC were eligible if they had progressed after first line treatment. Primary endpoint was objective response rate assessed by RECIST. Planned sample size is 30 patients over a period of 2 ½ years. Functional Assessment of Cancer Therapy-Lung (FACT-L) v4 questionnaire was used to assess the quality of life of patients on therapy.

Results: Twenty-two patients have been enrolled. 13 were men (59%) and 9 were women (41%). Fifteen patients were Hispanic (68%), four were Caucasian (18%), and 3 were African-American (13%). Median age was 55 years. Histologic subtypes were as follows: adenocarcinoma, 12; NSCLC not otherwise specified, 7; squamous cell carcinoma, 3. Nine patients had an ECOG performance status (PS) of 0 (41%) and 13 had a PS of 1 (59%). Two patients were never smokers. A total of 56 cycles have been administered (median 2, range 1 to 6). GEMOX was given as second-line therapy to 18 patients (81%), and as third-line to 4 patients (18%). Twenty patients are available for assessment of response. Two patients had a confirmed partial response (10%) and another eight had stable disease (40%). Two patients died on study from disease progression leading to respiratory and multi-organ failure. The following Grade 3 and 4 adverse events were seen in 2 patients each: fatigue, dyspnea, anemia, and multi-organ failure. Preliminary results of FACT-L analysis in 19 pts show improvement in Lung Cancer Subscale (LCS) score in 25% of the patients after 2 cycles of therapy.

Conclusions: Gemcitabine in combination with oxaliplatin is active and well tolerated as second and third line treatment for advanced NSCLC. Improvement of LCS score after 2 cycles suggests clinical benefit that is beyond the observed response rate of 10%.