1045 PUBLICATION

## Results after external radiotherapy in small cell lung cancer

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**Purpose:** A better clinical response has been achieved in patients with small cell lung cancer (SCLC) after combined chemotherapy and radiotherapy. In this study 171 patients were retrospectively analysed to evaluate the most effective and tolerated dose schedule for radiation of SCLC.

**Methods:** Between May 1984 and January 1998, 137 male and 34 female patients (median age 60.5 years, range 35–82) with SCLC were treated at our institution. 71 patients presented with limited disease (LD) and 100 patients with extensive disease (ED), 154 patients had received chemotherapy (mostly platin based) prior to radiation. The dose schedules were as follows: Group A (n = 43, superior vena cava syndrome) 30 Gy/3 Gy in 2 weeks, Group B (n = 86) 42.56 Gy/2.66.Gy in about 3 weeks and group C (n = 42) 50–60 Gy/2 Gy in 5–6 weeks.

**Results:** The median survival for LD and ED was 13.6 and 8.7 months, respectively. There was a significant difference in median survival between group A and group B and C, respectively. There was neither a significant difference in survival nor in toxicity between group B (RT: 3 weeks) and group C (RT: 5–6 weeks).

**Conclusion:** Considering that survival is poor in SCLC a tolerable dose schedule with higher single fraction and therefore shorter treatment time may be a benefit to patients life quality.

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## Carboplatin/vinorelbine is active and well tolerated in untreated locally advanced and metastatic non-small cell lung cancer (NSCLC) – Preliminary results

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**Purpose:** To determine the response rate, survival and toxicity of carboplatin/vinorelbine combination chemotherapy in unresectable locally advanced and metastatic non-small cell lung cancer (NSCLC).

**Methods:** Between 4/97 and 2/99, 25 chemo-naive patients (19 M, 6 F, mean age 61) received treatment with carboplatin AUC 5–6 on day 1, and vinorelbine 25 mg/m$^2$ on days 1, 8 and 15. Treatment was given every 28 days for 6 cycles unless progressive disease occurred. Nineteen patients had Stage IV disease, and six had Stage IIIB. One patient had ECOG PS 2; the remainder were PS 0 or 1. Eight patients had previously received radiotherapy (2 whole brain, 5 thoracic, 1 spinal).

**Results:** Eighteen patients were fully assessable with seven objective partial responses (7/18, 39%) or an overall objective response rate of 7/25 (28%; 95% CI 12–49%). Median duration of response was 7 months (range 4.5–13 months). Median time to progression was 2 months. Median survival was 4.5 months (95% CI 3–7 months). The median number of cycles completed was 2 (range 1–6). Day 15 vinorelbine was administered in 16% of cycles. Only two patients required dose reduction. Overall the treatment was well tolerated even in elderly patients. The main toxicity was myelosuppression. Twelve patients (48%) had WHO grade III/IV neutropenia, however, there were only three episodes of febrile neutropenia. Five patients required blood transfusion, one developed grade III thrombocytopenia, and one developed a rash. One patient stopped treatment because of grade IV autonomic neuropathy. No patient had significant nausea and vomiting. There were no treatment-related deaths.

**Conclusion:** This study is ongoing. These preliminary results indicate that the combination of carboplatin/vinorelbine has a similar response rate to standard cisplatin/vinorelbine (26%–30%; Wozniak et al, 1998, Le Chevalier et al, 1994) in unresectable NSCLC. However, it is better tolerated, avoiding the emesis of cisplatin. This regimen requires further evaluation as a more convenient and less toxic alternative to cisplatin/vinorelbine.

1047 PUBLICATION

## High-dose gemcitabine (HDG) in non-small cell lung cancer (NSCLC)

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**Purpose:** GEM is a few toxic cytostatic agent with known activity in NSCLC. We treated 28 pts. with GEM 2.000 mgrs/m$^2$ days 1, 8, 15 each 4 weeks. The reasons for no treating these patients with cisplatin-containing regimens were age, concomitant pathology with poor performance status including cardiopahty and neumopathy and empyema (1 case)

**Methods:** From September 1997 to February 1999 we treated 28 pts. with this schema. They were 24 males and 4 females. The median age was 68 years (range: 34–76). The histology was adenocarcinoma (14 cases), squamous cell carcinoma (12) and large-cell undifferenciated carcinoma (2). The TNM stage were III-A in 6 cases, IIIB (5), IV (13) with bone metastases in 6 cases, hepatic in 3, lung in 3 and 1 CNS metastases. In 2 cases they were locorregional recurrence after prior treatment (including chemo, RT, surgery or combination of all three), and in 2 cases the pts. had locorregional and metastatic disease. The PS of our pts. were ECOG-0 (1 case), 1 (12), 2 (12) and 3 (3).

**Results:** We administered 86 courses (from 1 to 7, with a median of 3). The toxicity according with OMS scales 3–4 were present in 15 courses (15/86 = 17%, CI 95% 9–25). The toxicity consist in neytropenia (6/86 = 7%, CI 95% 3–15), thrombopenia (1/86), asthenia (2/86). In 2 cases we had to discontinue our treatment because of ACVA (in all 2 cases the patient had previous ACVA). One patient died with abdominal sepsis without neutropenia. Twenty-three (23) pts. were evaluable for response. We obtained 5 (5/23 = 22%, CI 95% 8–44) objective responses (OR) (1 CR and 4 PR) and 10 stable disease (obtaining clinical benefit with decrease in PS in 3 of these 10 cases). Eight pts. progressed with therapy. All 5 pts. with OR did not have extrathroracic disease. We have not responses in metastatic disease.

**Conclusions:** Gemcitabine is a well tolerated agent with a moderate activity. The activity in this setting seems to be not better than with lower doses.

1048 PUBLICATION

## Combination chemotherapy with carboplatin (CBDCA), docetaxel (DOC) and gemcitabine (GEM) in advanced non-small cell lung cancer (NSCLC). A phase II study

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**Purpose:** This study was conducted to evaluate the efficacy and toxicity of the combination of CBDCA, DOC and GEM in advanced NSCLC.

**Methods:** Forty-five chemotherapy (CT) – naïve patients (pts) with NSCLC were treated on an out-patient basis with CBDCA AUC 5 I.V. and GEM 800 mg/m$^2$ on day 1 and DOC 75 mg/m$^2$ I.V. with standard oral steroids premedication and GEM 800 mg/m$^2$ I.V. on day 8. G-CSF was given prophylactically from days 3–6 and 10–16. CT was repeated every 4 weeks. Patient's median age was 58 y and the ECOG PS 0 in 16 pts, 1 in 17 and 2 in 12. Nine (20%) pts had stage IIIb disease and 36 (80%) stage IV. The histology was mainly squamous cell carcinoma (51.2%) of poorly differentiated (37.8%).

**Results:** A CR was achieved in 4 (9.75%) pts and a PR in 17 (41.6%) with an ORR of 51.2%; SD and PD were observed in 7 (17.03%) and 13 (31.7%) pts, respectively. The median duration of response was 7.6 mos and the median TTP 8.1 mos. The median survival (S) was 13.5 mos and the actuarial 1-year S 46.34%. G3/4 anemia and thrombocytopenia occurred in 17.7% and 28.8% of pts, respectively. G3/4 neutropenia occurred in 21 (46.6%) pts and 6 (13.3%) of these were complicated with fever. Alopecia was universal. G3 diarrhea occurred in 4 (8.8%) pts, G3/4 neurotoxicity in 10 (22.2%) and G2/3 allergic reactions in 3 (6.6%). There were no treatment related deaths. Six (13.2%) pts required a dose reduction and 2 of these 2 dose reductions.

**Conclusion:** The combination of CBDCA, DOC and GEM is an active regimen in advanced NSLCLC with moderate toxicity.

1049 PUBLICATION

## A phase I–II study with carboplatin (C) and weekly paclitaxel (P) in advanced NSCLC

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The association of C and P is a well tolerated outpatient regimen with a remarkable activity in inoperable NSCLC. In order to increase dose-intensity of this combination, a trial with a fixed dose of C AUC = 6 (d 1, 28) and escalating doses of weekly P as 1 hour infusion (d 1, 8, 15, 28) was started.