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Second line treatment of non-small cell lung cancer with paclitaxel and gemcitabine

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Purpose: To evaluate the tolerability and efficacy of the paclitaxel and gemcitabine combination in patients with NSCLC who failed first-line cisplatin-based chemotherapy.

Methods: Eligibility criteria included patients with histologically confirmed stage IIIB or IV NSCLC, with measurable disease, WHO performance status 0–2, adequate hematologic parameters and adequate renal, hepatic and cardiac function. Patients received gemcitabine (900 mg/m^2) on days 1 and 8 (30 min infusion), while paclitaxel (175 mg/m^2) was given on day 8 (3 hr infusion) after appropriate premedication. Granulocyte colony-stimulating factor (G-CSF; 5 μg/Kg, SC) was given on days 9–15. Treatment was repeated every 3 weeks until disease progression.

Results: Twenty six patients were enrolled (3 with stage IIIB and 23 with stage IV disease). Twenty-two patients were assessable for toxicity and 14 for response (12 patients too early). Grade 3/4 granulocytopenia occurred in 2 patients (9%); grade 2 anemia and thrombocytopenia was observed in 7 (32%) and 2 (9%) patients respectively. Grade 2/3 neurotoxicity and fatigue were observed in 6 (27.2%) and 8 (36.4%) patients, respectively. Grade 2 nausea and vomiting was observed in 12 patients (55%), mucositis in 3 (13%) and diarrhea in 5 (23%). One complete (7.1%) and 3 partial responses (21.4%) were observed for an overall response rate of 28.5% (95% C.I.: 4.9–52.2%). The median duration of response was 4.5 months and the median surgical was 8 months. All responses occurred in patients with squamous cell carcinoma. The median dose intensity was 579 mg/m^2/week for gemcitabine and 54.5 mg/m^2/week for paclitaxel, (96.5% and 94% of the protocol planned doses, respectively).

Conclusions: These preliminary data suggest that the paclitaxel-gemcitabine combination is a well tolerated and active treatment of NSCLC for patients who failed or relapsed cisplatin-based chemotherapy.

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Phase II study of taxotere/carboplatin with pharmacokinetics and -dynamics in NSCLC for downstaging in stage III B and palliation in stage IV

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Purpose: The toxicity, pharmacokinetics and intracellular DNA-adduct formation of the combination taxotere/carboplatin was studied in a phase II treatment protocol for advanced NSCLC. Secondary end points were efficacy and operability (stage IIIB).

Methods: Ten pts with functionally operable stage IIIB (stratum 2) were enrolled to receive 4 cycles of taxotere 100 mg/m2 d1 and carboplatin AUC 7.5 d2 and subsequently evaluated for surgery. Ten pts with NSCLC stage IV (8 pts) or functionally inoperable stage IIIB (2 pts.) (stratum 1) were enrolled to receive a maximum of 6 courses of the same therapy except for cycle 2 where taxotere was given on d2 and carboplatin on d1. All patients were treated on an outpatient basis with cytokine support starting after cycle 1.

Results: Of 8 evaluable stratum 1 pts, 1 had CR, 5 had PR (OR 75%) and 2 had PD. Of 8 evaluable stratum 2 pts, 6 had PR (OR 75%), there was 1 toxic death after cycle 1 and 1 exclusion because of capillary leak. Pharmacokinetic and -dynamic data as well as histopathologic response will be presented at the meeting.

Conclusion: Taxotere/carboplatin is a highly effective regimen for downstaging in NSCLC. Toxicity is acceptable and treatment can be given on an outpatient basis.

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Pretreatment predictors of metastatic potential verified at autopsy in patients (pts) with inoperable non-small cell lung cancer (NSCLC)

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Purpose of Study: 1. Describe the metastatic pattern at autopsy in pts with inoperable NSCLC. 2. Evaluate for possible influence of pretreatment variables or response.

Methods: Pretreatment variables and response to chemotherapy were recorded in 337 pts treated in 8 phase II trials (1985–1993). In case of death, autopsy reports were reviewed and organs with metastatic involvement recorded.

Results: 51 autopsies were performed out of 334 expired pts (autopsy rate 15%). Among autopsied pts, female/male ratio was 20/31, median age 56 years (range 36–71), response rate to chemotherapy 8% and median survival 88 days (range 3–899). Histologic types were: Adenocarcinoma 31 pts (60%), squamous cell carcinoma 9 pts (18%), large cell carcinoma 9 pts (18%) and unclassified NSCLC 2 pts (4%). Most commonly involved metastatic sites at autopsy were: Mediastinal lymph nodes 84% of cases, pleura 51%, liver 47%, bones 34%, brain 32%, pericardium 29%, adrenals 29%, and contrelateral lung 24%. Median number of involved organs were 5 (range 0–16), with a median of 3 intrathoracic (range 1–8) and 2 extrathoracic sites (range 0–11). Pts with initial metastatic disease (stage IV) had also more metastases at autopsy than stage IIIa+b pts, both totally (median 6 sites, range 3–16 vs. 4, range 0–15, p = 0.03) and extrathoracic (median 3 sites, range 0–11 vs. 1, range 0–7, p = 0.004).

Conclusions: Age, gender, pretreatment LDH, performance status, response to chemotherapy or survival duration did not predict subsequent metastatic distribution. All histologic types of NSCLC had similar metastatic potential and similar distribution of metastases at time of death, emphasizing the rationale for treating those patients as one clinical entity.

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Repeat mediastinoscopy after neo-adjuvant chemotherapy in stage III (N_2) non-small cell lung cancer (NSCLC)?

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Study Objectives: A) To evaluate the prognostic effect of tumor eradication in mediastinal lymph nodes after neo-adjuvant chemotherapy (NAC) in stage III (N_2) NSCLC. B) To determain the usefullness of CT to predict the presence of lymph node metastasis in the pre-operative situation.

Methods: 24 patients with stage III (N_2) NSCLC were treated with NAC, after which responsers underwent resection. Irradiation of the mediastinum was started after operation. Prediction of mediastinal lymph node (MLN) metastasis jugded on node size by evaluation of CT-scans was compared with histological specimens before and after chemotherapy, and survival was related to node response.

Results: Complete response in MLN resulted in significant longer mean survival time (22.9 +/– 6.5 months) compared to patients with residual tumor in MLN (9.8 +/– 7.4 months, p = 0.004). Incomplete MLN-response resulted in comparible survival as patients with progression. The pre-operative CT was of low value to predict the MLN-status (accuracy: 59%, negative predictive value 38%).

Conclusion: Adequate re-staging can prevent unnecessary operations. Although generally used to stage MLN, CT is unreliable after NAC. Repeat mediastinoscopy seems to have better predictive value with an acceptable morbidity, when performed by an experienced surgent.