

ing, resections were planned 4-6 weeks after completion of the neoadjuvant therapy.

Results: 55 patients have been treated and complete data are available for the first 41 patients (31 male, median age 57 years (32-70), 12 IIIA, 29 IIIB). Grade III and IV toxicity during chemotherapy or chemo-radiation occurred in 18 and 2 patients, respectively (6x hematol., 12x esophagitis, 1x skin, 1x kidney). At the time of restaging an overall response of 46% (15% CR) was observed. 26 patients underwent an operation and R0 resections could be achieved in 19 patients. Median survival of all patients was 22 months. 1 year survival in operated and non operated patients was 86% and 31%, respectively ($p < 0.01$). Distant metastases have been observed in 12 cases (7 brain, 4 bone, 1 liver).

Conclusion: The tested neoadjuvant regimen exhibits tolerable toxicity and considerable activity. The predominance of brain metastases in the pattern of failures indicates the need for adjuvant brain irradiation that will be used for subsequent patients.

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Taxol, Gemcitabine and Vinorelbine, a very active platinum free triplet in naive patients with Non Small Cell Lung Cancer

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Although cisplatin is still considered the most active chemotherapeutic drug in the treatment of advanced NSCLC, newer cytotoxic agents have shown promising results. Moreover, the side effects of cisplatin combinations often overcome the benefit from chemotherapy and quality of life of treated patients is usually worsened. The aim of this study was to determine the efficacy and the safety of a three drug combination non containing cisplatin in the treatment of advanced NSCLC. Since December 1998, 41 pts affected with stage IIIB or IV NSCLC, not previously treated with chemo or radiotherapy were enrolled into the study. Paclitaxel, Gemcitabine and Vinorelbine (TGV) were given at dosage of 70 mg/m², 1000 mg/m² and 25 mg/m² respectively, on days 1 and 8 of a 3 week schedule. All patients entered on study were considered evaluable (intent to treat) and received a total of 189 courses of chemotherapy (median 4,6 per patient). Male/female ratio was 34/7; median age was 60 yrs (range 43-73), PS was 0-1 in 31 pts and 2 in 10 pts; stage was IIIB or IV in 16 and 25 pts respectively; 12 pts had adenocarcinoma, 26 squamous and 3 undifferentiated histologic type; 14 pts (34%) complained a weight loss >10% in the last 6 months. Overall, we observed PR in 23 pts (56%) and CR in 4 pts (10%) respectively. It must be emphasized that 13/16 (81%) pts with stage IIIB responded as compared to 14/25 (56%) stage IV pts. Median time to treatment failure was 26 weeks (range 3 to 47) and median survival 13 months (range 1 to 19). One year survival was 54%. Relative dose intensity were 68% for paclitaxel, 85% for gemcitabine and 78% for vinorelbine respectively. With regard to toxicity, grade 3-4 neutropenia was observed in 11 and 7 pts (total 44%), g3 anemia in 4 pts (10%) and g3-4 thrombocytopenia in 3 (7%). The most relevant non-hematological toxicity was asthenia which was observed in 12 (29%) pts (9 pts G 1-2 and 3 pts with grade 3). Alopecia was almost universal whereas nausea and vomiting practically absent. One patient showed hypersensitivity reaction after the first paclitaxel administration and continued on protocol without this drug. In conclusion, the combination of paclitaxel, gemcitabine and vinorelbine is very active in NSCLC (66% response) with tolerable toxicity profile.

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The combination of gemcitabine and oxaliplatin (GEM-OXAL) is feasible in patients with poor prognosis advanced non-small cell lung cancer (NSCLC). Results of a phase II study

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Background: Oxaliplatin (OXAL) is active in non-small cell lung cancer (NSCLC) and escapes the mechanisms of resistance of Cisplatin (CDDP) mediated by the mutations of the Mismatch Repair (MMR) genes. In addition OXAL and Gemcitabine (GEM) show in vitro schedule-dependent synergism.

Aims: To define the clinical activity and tolerability of GEM-OXAL combination in NSCLC patients (pts).

Study Design and Schedule: We designed a phase II study; GEM (1000 mg/m² in 30'; days 1 and 8) infusion was immediately followed by OXAL (65 mg/m² in 2h, days 1 and 8); the schedule was repeated every 21 days for six cycles. The assessment of response was performed after the third and sixth cycle.

Characteristics of Patients: From May 2000 to April 2001, 28 pts with poor prognosis advanced NSCLC were accrued; until now a total of 103 cycles were performed. There were 21 males and 7 females; median age was 65 years (29-76); histology subtype was adenocarcinoma in 15 pts, squamous cell carcinoma in 9 and NSCLC NOS in 4. Tumor stage was IV in 17 pts and IIIB in 11 pts; PS (ECOG) was 2 in 13 pts, 1 in 5 and 0 in 10; all pts were symptomatic and 5 pts had been previously treated with CDDP or carboplatin.

Results: In April 2001 19 pts were evaluable for response after at least 3 cycles (5(26%) of whom obtained PR, 1 MR, 6 SD and 7 PD. Twenty-six pts were evaluable for toxicity after at least one cycle; the toxicity was low and mainly hematological: 5 pts had Gr4 and 2 pts Gr3 thrombocytopenia; 1 pt had Gr4 and 4 pts Gr3 leucopenia; 1 pt had Gr4 and 3 pts Gr3 neutropenia; 3 pts had Gr3 anemia. Three pts developed Gr2-3 hepatic toxicity with increase of GOT/GPT. One pt experienced Gr3 and 2 pts Gr1 neurotoxicity.

Conclusions: GEM-OXAL combination seems to be well tolerated and active in poor prognosis advanced NSCLC. The definitive results of the study and the correlations between the immunohistochemical evaluation of the MMR status (MSH2 and MLH1 genes) and the clinical data will be presented.

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A new irradiation technique for lung cancer: Patient's self-breath-hold and self-switching radiation-beam on and off without any respiratory monitoring devices

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Purpose: 1) To compare the reproducibility of tumor-position under a breath-hold by a patient's self-estimation with that under a breath-hold by a radiation technologist's instruction. 2) To evaluate the reproducibility of a tumor position in the radiation field with portal images under patient's self-breath-hold and self-switching radiation beam with a newly developed switch which was connected directly to the console box of Linac (EXL-15DP: Mitsubishi Electric, Japan) and enabled patients to turn radiation beam on and off. **Methods:** 1) Twenty patients with lung cancer were taught sufficiently how to hold the breath at a same inspiration phase with showing a fluoroscopy of respiratory motion before evaluation. Three series of CT were obtained with 2mm-thickness in the vicinity of the tumor. Differences of tumor position were measured using CT analysing menu. 2) Ten real-time portal images were taken for each patient during irradiation under a patient's self-breath-hold and self-switching of radiation-beam, and the accuracy of reproducibility of the tumor position was visually evaluated. **Results:** The average of maximum differences of the tumor position of 20 patients under the breath-hold by a radiation technologist's instruction was 3.0mm in cranio-caudal direction, 2.1mm in antero-posterior direction and 2.3mm in right-left direction. And that under the breath-hold by a patient's self-estimation was 2.3mm in cranio-caudal direction, 1.4mm in antero-posterior direction and 1.4mm in right-left direction, respectively. There was statistically significant difference between two methods of breath-hold. All portal images of 20 patients had a visually satisfactory accuracy of tumor position in the radiation field with a difference less than 3mm between a planned position and actual tumor positions. **Conclusion:** The reproducibility of tumor position under patient's self breath-hold without any respiratory monitoring devices had a satisfactory accuracy with a difference of tumor position less than 3mm in all directions. The method of breath-hold by a patient's self-estimation was more accurate than that by a radiation technologist's instruction. Our newly developed switch which enabled patients to the radiation-beam on and off was useful with a good reproducibility under a breath-hold at patient's pace. This new irradiation system is simple and useful for irradiation of lung cancer with reduced PTV and a satisfactory reproducibility.