T 45 mgr/m2/iv weekly during the 7 weeks of treatment; Gr-2 received only radiation therapy (60-65 Gys, 200 cGy/day over 6 weeks). 4 p could not be evaluables, 55 p were evaluables for response and 56 p for toxicity.

Results: Upon TCG induction chemotherapy: 1 CR and 37 PR (RR 69.1%;CI95%:56-80), 10 SD (18.1%) and 7 PD (12.8%).7 p went to surgery: 2 pCR, 2 pPR and 3 pSD. 17 p in Gr-1 completed the consolidation treatment with 4 CR, 9 PR, 1 SD and 3 PD (RR 76.5%) and 14 p in Gr-2 with 5 CR, 7 PR and 2 PD (RR 85.7%). At a median follow-up of 9.3 months, the median survival were 16.5 mo (Gr-1 13.7 mo and Gr-2 14.5 mo) and 1-year survival rate of 65% (Gr-1 69% and Gr-2 62%). A total of 168 cycles of TCG were administered (3 per p), with the hematologic toxicity (NCI-CTC) per p Grade 1-2/3-4 (%) as follows: neutropenia 30.3/42.8; anemia 59/12.5; thrombopenia 28.5/25; there was 1 death from toxicity and 10 hospitalisations for complications. The main toxicities (RTOG) in consolidation treatment were: in Gr-1: g1/2 esophagitis in 5/6 p, g 1/2 pneumonitis in 3/3 p, g1/2 neurophathy in 2/5 p; in Gr-2: g1/2 esophagitis in 2/2 p and g1 pneumonitis in 2 p.

Conclusions: The TCG scheme of induction chemotherapy is active against stage III NSCLC with moderate toxicity. A larger number of patients and a longer follow-up will be required to allow final conclusions to be drawn as to the posible difference between the consolidation treatment groups.

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UFT plus cisplatin with concurrent radiotherapy for locally advanced non small-cell lung cancer: a multiinstitutional phase II trial. Cis-UFT-RT Study Group

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Purpose: A multiinstitutional phase II study of combined-modality treatment consisting of uraciland tegafur (in a molar ratio of 4:1 [UFT]) plus cisplatin (Platinol) and concurrent radiotherapy was conducted to conclude the high activity of this regimen in patients with locally advanced non small-cell lung cancer.

Methods: Eligible patients with cytologically or histologically confirmed, unresectable stage III non-small-cell lung cancer received UFT (400 mg/m2 orally on days 1 - 14, 29- 42) and cisplatin (80 mg/m2 intravenously on days 8, and 29). Radiotherapy, with a total dose of 60 Gy, was delivered in 30 fractions on days through 40.

Results: Among the 58 patients entered(Stage IIIA 12; Stage IIIB 46), 46 experienced good responses (CR 1; PR 45)(79.3%; 95% confidence interval, 67.2% to 87.7%). Hematologic toxicity was moderate. Grade 3 leukopenia occurred in 11 patients (19%), but grade 4 hematologic toxicity was observed in 1 patient. Grades 3 or 4 nonhematologic toxicities were reported in 1 patient with esophagitis.

Conclusion: These observations suggest that oral UFT plus cisplatin with concurrent radiotherapy can be safely administered to patients with locally advanced non-small-cell lung cancer with mild toxities. The demonstrated antitumor activity is high, making this combined-modality treatment worthy of further investigation in comparison with other cisplatin-based regimens in a prospective randomized trial.

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Preventive epoetin a (EPO) use in the treatment of advanced nsclc: an AIPO oncology study group multicenter trial

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Purpose: Anemy is an important problem which we meet in the treatment of neoplasms. Meanly it reduces drug dose intensity and influences patient quality of life. Epoetin a can improve hemoglobin level but its use, until now, is reserved to correct anemy. Now we try to use Epoetin a to prevent anemy and improve drugs tolerance and quality of life in patients in chemotherapy for advanced NSCLC.

Methods: We have randomised, until now, 64 patients in chemotherapy for advanced NSCLC in two arms when hemoglobin level is 12 g/dl. or less: the group in arm A was treated with Epo a 150 u.i./kg. every other day for three months. Arm B is the control group without Epo a: but, if the hemoglobin level becomes less than 10 g/dl. patient comes out from the trial and will be treated with Epo a. We have evaluated hemoglobin levels, chemotherapy dose intensity and quality of life at 0 time, after one and three months. QoL was measured by patient completion of two scale, FACT-G and FACT-An, which was translated and adapted by us to Italian people.

Results: At this moment only 36 patients, 18 for arm, are evaluable. In arm A the differences between the hemoglobin level of baseline and third month control show an increasing of values ($P<0,093$); the same control in arm B shows a decrease in hemoglobin level, statistically significant ($P<0,0004$). Dose intensity in arm A reaches 95%, in arm B 65%. Scores of the evaluation scale in arm A are uniform in the time; in arm B scores show statistically significant increasing between first and following evaluations.

Conclusions: At this moment our findings show that preventive use of Epoetin a is able to improve tolerance of NSCLC patients to chemotherapy, measured by hemoglobin levels and dose intensity. QoL appeares to be better during the time of treatment too.

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Phase i/ii study of docetaxel(DOC) and carboplatin(CBDCA) with concurrent radiotherapy in patients with stage III unresectable non-small cell lung cancer(NSCLC), preliminary results

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Purpose: Concurrent chemoradiotherapy plays an important role in the treatment of stage III NSCLC. Both DOC and CBDCA have demonstrated activity as radiation sensitizers in preclinical studies. We conducted a phase I/II study to determine the maximum tolerated dose (MTD) and recommended dose (RD) of DOC and CBDCA when administered with concurrent thoracic radiotherapy (Phase I), and subsequently, to evaluate the efficacy and toxicity of the treatment regimen at the RD (Phase II).

Methods: Twenty three patients with stage III unresectable NSCLC were enrolled in the phase I study. DOC and CBDCA were administered bi-weekly (D1, 15, 29, 43, 57, 71) at the following DOC (mg/m2)/CBDCA (AUC) dose levels: 20/2.5, 20/3.0, 30/2.5, 30/3.0, and 40/3.0. Concurrent thoracic radiotherapy was performed in 2Gy daily fractions to a total dose of 60Gy. DLT was defined as grade 4 hematological toxicity, or grade 3 or 4 nonhematological toxicity. Three to six patients were entered at each dose level. Dose escalation continued until greater than one half of patients developed DLT. After determing the MTD and RD, the phase II study was initiated to evaluate the efficacy and toxicity at the RD.

Results: The MTD was DOC 40mg/m2 and CBDCA AUC 3. To date, 19 patients have been treated in the phase II study. An overall response rate of 83%(95% C.I.: 56-96%) was observed in 18 evaluable patients (15 PR, 2 NC, 1 PD).

Conclusions: Combined chemotherapy of bi-weekly DOC and CBDCA with concurrent radiotherapy in stage III NSCLC was well tolerated. The preliminary efficacy data are promising. Updated results will be presented.

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Neoadjuvant chemo-radiation with paclitaxel/carboplatin in stage III non small cell lung [NSCLC] patients

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Background: Neoadjuvant chemo-radiation has been shown to induce significant down staging and improved resectability in stage III NSCLC. The reported high response rates of paclitaxel/carboplatin were rationale to test the efficacy of these drugs in combination with radiotherapy in the neoadjuvant setting in a phase II trial.

Methods: Patients (>17 to <70 years, KPS >70%) in stage III NSCLC (staging included CT-thorax/abdomen/cranium, PET, and mediastinoscopy) without supraclavicular lymph node involvment qualified for the study. Paclitaxel 100 mg/m* and carboplatin AUC 2 were administered at day 1, 8, 15, and 22 followed by hyperfractionated/accelerated radiotherapy starting at day 43 (2x1.5 Gy/day, 5x/week to 45 Gy) with simultaneous paclitaxel (50 mg/m*) and carboplatin (AUC 2) at day 44, 51, and 58. Erythropoetin (3x 150 I.E./kg/week) was given at a Hb $\leq$10.5 g/100 ml. After complete restag-

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). Grad 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 resistence 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 immediatly followed by OXAL (65 mg/m2 in 2h, days 1 and 8); the schedule was repeated every 21 days for six cycles. The assesment 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); hystology 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 patientís self-estimation with that under a breath-hold by a radiation technologistís instruction. 2) To evaluate the reproducibility of a tumor position in the radiation field with portal images under patientsí self-breath-hold and self-switching radiation beam with a newly developed switch which was connected directory 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 patientís 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 technologistís 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 patientís 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 patientís 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 patientís self-estimation was more accurate than that by a radiation technologistís 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 patientsí pace. This new irradiation system is simple and useful for irradiation of lung cancer with reduced PTV and a satisfactory reproducibility.