NSCLC, measurable tumor, no previous chemotherapy, KPS ≥60, age ≤75, normal hematological, hepatic and renal functions, no brain or leptomeningeal involvement and signed informed consent. Fifty-one patients have been included: 3 were not eligible, the characteristics of the 48 remaining pts are: 44 males, 4 females; mean age: 54 years (range 34–75); stage IIIB: 13%, stage IV: 87%; they received a mean of 4 cycles (range 1–6). Among these 48 pts, 1 CR and 13 PR (29%) were observed, including 9 PR confirmed today by an independent panel, lasting from 15+ to 31+ weeks. Main toxicities (G 3–4) were: febrile neutropenia: 5 pts, documented sepsis: 5 patients. No toxic death was reported. As a result of using routine premedication, previously reported side effects were considerably lessened. Based on this preliminary analysis combination of docetaxel 75 mg/m^2 and cisplatin 100 mg/m^2, indicates an interesting result which should deserve other investigations of this drug combination.

1097 PUBLICATION

THE INFLUENCE OF SEX, AGE AND HISTOLOGY ON TREATMENT RESULTS OF RADICALLY TREATED PATIENTS WITH LOCALLY ADVANCED, NON-SMALL CELL LUNG CANCER RADIATED WITH CURATIVE INTENT

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In prospective, randomized study the influence of sex, age and histology on the prognosis and survival of 190 patients with inoperable, non-small cell lung cancer was examined. The patients have been treated with curative radiotherapy with tumour dose of 60 Gy, accomplished in two different radiation techniques: split course and continuous course with reduced additional field. There was not a statistically significant influence in obtained response and survival according to prognostic factors mentioned above. Three years survival rate was statistically higher in radically treated women (26.3%) compared with radically treated men (11.6%). In the age group of 50 to 59 years three years survival rate was 17% and it was higher compared with survival rate achieved in the other age groups. The obtained objective response had a significant influence on survival rate independently of histology.

1098 PUBLICATION

EXPRESSION OF SEVERAL BIOLOGIC MARKERS AS PROGNOSTIC FACTORS IN PATIENTS WITH NON-SMALL CELL LUNG CANCERS

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Despite modern diagnostic, staging, and therapeutic advances, esp. with molecular biologic techniques, the 5-year survival rate of all cases of lung cancer does not exceed 15%. With better understanding of tumor biology, one may improve survival through proper treatment. Here we present the clinical significance of several biologic markers as prognostic markers in patients with non-small cell lung cancers. The survival has correlated with the expressibility of proliferative cell nuclear antigen (PCNA), epidermal growth factor receptor (EGFR), p53 and/or blood group antigen A (BGAA) using immunohistochemistry in 46 cases patients with non-small cell lung cancers. The results were as follows: (1) The expression of BGAA was correlate with better survival in median survival and in 2-year survival and that of PCNA was correlated with worse survival in median survival and 2-year survival rate. (2) The expression of EGFR or p53 was not valuable to predict prognosis in non-small cell lung cancers. (3) With simultaneous applications of PCNA, EGFR and p53 immunostain, the patients with 2 or more negative expressions showed better prognosis than the patients with 2 or more positive expressions. In conclusion, it is suggested that the expression of blood group antigen may be a positive prognostic factor and that of PCNA may be a negative prognostic factor and also, the combination of expressions of PCNA, EGFR and p53 may be used as a negative prognostic factor.

1099 PUBLICATION

CISPLATIN (CDDP), 5-FLUOROURACIL (5FU) AND VINORELBINE (NVB): A PHASE II STUDY IN ADVANCED NON SMALL CELL LUNG CANCER (NSCLC)

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Thirty-three patients, 25 males, 8 females, median age 55 years (37–70), with histologically proven measurable (CT scan) NSCLC were treated at Institut Curie with a three drug combination chemotherapy. The regimen consisted of CDDP 25 mg/m^2 continuous infusion (CI) days 1 to 5, 5FU CI 600 mg/m^2 days 1 to 5 and NVB 25 mg/m^2 on days 1 and 5. Cycles were repeated every 28 days.

Staging of these unresectable or inoperable tumors was as follows: stage IIIA (5 pts), stage IIIB (15 pts), stage IV (13 pts). PS 0–1 (26), PS 2 (7). 94 courses of chemotherapy were delivered. Response evaluation was done after 2–3 cycles. One patient died of complications from an ischemic cerebrovascular stroke after the third cycle. 32 pts were evaluable. Partial response was achieved in 11/20 stage III pts (55%) and in 7/12 stage IV pts (58%). Nine patients had a minor response or stable disease and 2 patients progressed. WHO grade 4 toxicities were leucopenia 31%, thrombocytopenia 4%, mucositis 4%. The tolerance is acceptable and the overall response rate is encouraging.

1100 PUBLICATION

CONCURRENT DAILY CHEMOTHERAPY WITH HYPERFRACTIONATED THORACIC IRRADIATION IN STAGE IIIA & B NSCLC

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In January 1993 we initiated a pilot study of concurrent daily chemotherapy with hyperfractionated thoracic irradiation in Stage III NSCLC. Twenty-four patients were entered on study. The following were the demographics: 15 males and 9 females; median age 62 (35–77); mean performance status 0; histology—10 squamous, 3 adeno, 11 large cell carcinomas; stage—11 with IIIA, 12 with IIIB, 1 with IV. Chemotherapy consisted of CDDP 3 mg/m^2 daily (4 pts), 5 mg/m^2 daily (1 pt) and 6 mg/m^2 daily (19 pts), with weekly vinblastine 2 mg/m^2 (9 pts). Hyperfractionated thoracic irradiation 60 Gy in 40 fractions over 4 weeks at 1.5 Gy b.i.d. Four weeks post concurrent chemo-irradiation, 3 cycles of CDDP 75–80 mg/m^2 and vinblastine 8 mg/m^2 q 21 days were given. Overall response rate 18/24 (75%), CR 7/24 (29%), PR 11/24 (46%). Median time to progression 12.4 months, median survival 17.3 months. The major toxicity was esophagitis. The toxicity will be presented in detail.

1101 PUBLICATION

THE NEW POSSIBILITIES OF THE AUTO-LYMPH CHEMOTHERAPY NON-SMALL CELL LUNG CANCER

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The original Auto-lymph chemotherapy (ALCT) method includes extra-corporal incubation of the lymph, derived from the ductus thoracicus, with 120–130% of VAM, CAM, CAF, FEP doses. The reinfusion of the mixture leads to considerable treatment effects. The ALCT method was used in 47 lung cancer patients (27 with stage IIIB and 20—stage IV of disease), with 76.6% of marked partial tumor regressions and not a single case of progression.

As it was found, the regimen: 5-Ftoruracil 750 mg/m^2—1, 2, 3 days; Vepesid 100–150 mg/m^2—1, 2, 3 days; CDDP 100–120 mg/m^2—4th day—turned to be the most effective. This regimen was used in the treatment of 10 patients (6 with stage IIIB and 4—stage IV of disease), with 50.0% of marked partial tumor regressions. The investigation of ALCT-effect revealed the improvement of the immune status' parameters, the signs of immune stimulation. (An increase in the level of IL-I; IL-2; IL-6; TNF. FGA-response stimulation.) Cytotoxic activity of lymphocytes from the lymph (LL) in relation to transferred pulmonary carcinoma cells with the use of MTT-assay. The LL cytotoxicity revealed 1.5–3.0 fold increase after incubation with 5-ftoruracil (1500 mg/l) and vepesid (200 mg/l), with the maximal activity at the 3rd–5th day. Then, the activity decreased and turned to the initial level by the end of the third week.

The first attempts of LL (immune) *in vitro* stimulation between the ALCT courses by means of native IL-2 with the dose 100 IE per 1 ml of the auto-lymph: as it was found, there was more than 50% increase in LL-activity, as well as in improvement in the course of the treatment.

1102 PUBLICATION

LACK OF PROGNOSTIC SIGNIFICANCE OF IMMUNOHISTOCHEMICAL DETECTION OF P53 IN NON-SMALL CELL LUNG CANCER (NSCLC)

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The aim of this study was to establish whether immunohistochemical detected expression of p53 protein is related to prognosis in NSCLC. From 1984 to 1991 tissue samples were obtained from 186 surgical treated patients with NSCLC (squamous cell = SQ 104; adenocarcinoma = AD 59; large cell carcinoma = LA 22). The protein-product of the tumor suppressor gene p53 was analyzed on cryostat sections using the peroxidase Labelled Strept-Avidin-Biotin technique. P53 protein was visualized by the monoclonal antibody DO7 (DAKO), the percentage of tumor cells with nuclear staining (grade 0, grade 1 = 1–29%, grade 2 = 30–59%, grade 3 = 60–100%) was estimated and results were correlated with clinical characteristics. Grade 3 expression was found in 45% of tumors. p53 expression was neither correlated to tumor size, nodal status, stage or survival.

p53 may be important in the carcinogenesis of lung cancer but of little significance in established tumors.

1103 PUBLICATION

LUNG CANCER AT DIAGNOSIS AND RESPIRATORY INFECTIONS

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The prevalence of pulmonary infections in lung cancer at diagnosis was investigated in 96 patients submitted to bronchoscopy showing endobronchial tumor. Bronchoalveolar lavage (BAL) was carried-out instilling 60 ml of steril normal saline; The fluid recovered was immediately cultured for quantitative microbiological analysis. 42 micro-organisms (m.o.) were cultured from the BAL fluids of 33 patients (34.3%). 50% were Gram– 33% Gram+, 17 other m.o. Haemophilus species were the most frequent Gram– Staphilo coccus Aureus the most frequent Gram+. No relationship was found between respiratory infections and stage of the disease, performance status, histologic type, immunoregulatory ratio and serum lymphocyte subsets.

A quantitative BAL culture may be useful in patients with lung cancer at diagnosis, as respiratory infections are frequent and, if unrecognized and untreated, can become a risk factor when immunocompetence is impaired by chemotherapy or advancement in the stage of malignancy.

1104 PUBLICATION

(LACK OF) CORRELATION BETWEEN CARBOPLATIN (CBDCA) DOSE AND TREATMENT OUTCOME IN SQUAMOUS CELL BRONCHOGENIC CARCINOMA (NSCLC)

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In a prospective study 160 untreated patients with clinical stage IIIb and IV NSCLC were randomized to receive vindesin-mitomycin C-cisplatin or vindesin-mitomycin C—CBDCA (at fixed dose of 500 mgsqm). The drug free interval was 4 wks and patients were supposed to receive 6–8 cycles. CBDCA group obtained an response rate of 38% with median survival 6.2 mo. and experienced relatively mild toxicity. Received dose intensity (DI) for CBDCA was calculated to be 91% of planned DI. The treatment outcome was analyzed by the influence of CBDCA DI in respect of optimal individual dose calculated by Egorin, Calvert and Chatelut (ESMO Lisbon) formulas. Coefficients of variation between the dose of CBDCA based on body surface area and individual dose obtained by Calvert and Egorin formula were 30 and 40% respectively. Patients with PD received approximately 15% less of optimal dose compared to the patients with CR only, but small numbers of CRs do not allow firm conclusion. Due to broad range of pretreatment platelet count, Calvert formula might not be suitable for optimal dose finding in NSCLC patients. It is concluded that DI-outcome correlations are not consistent for CBDCA in NSCLC. It is of questionable value to test this hypothesis in a prospective manner due to lack of sensitivity of NSCLC to chemotherapy agents available.

1105 PUBLICATION

A SURVEY ON CLINICAL PRACTICE WITH HYPERFRACTIONATED RADIOTHERAPY (HFX) AND CONCOMITANT CISPLATIN IN STAGE III NON SMALL CELL LUNG CANCER

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To define the toxicity and effectiveness of concomitant Chemotherapy (CTH) and HFX in Non Small Cell Lung Cancer (NSCLC), a phase I/II study was conducted with Cisplatin 4 mg/day (16 mg/mq/week) given during two daily fractions irradiation (1.2 Gy, 6 hours apart) to 69.6 Gy in 58 fractions in a 6 weeks time. Thirty-six eligible patients (PTS) (81% males, 58% squamous, 25% adeno, 17% NSC—carcinomas, 53% stage III B) were treated in 5 different lospitals. Protocol treatment was completed in 56% of the PTS; in 81% the total radiation was > 66 Gy; in 69% Cisplatino total dose was >64 mg/mq. Acute toxicity was (EORTC scale): 17% esophagitis grade (gr) 3, 31% gr 2—upper GI 3% gr 3, 11% gr 2—hematologic 11% gr 2–3. There was a subacute lung toxicity death. Median survival time was 14 months (range 6–21); 25 PTS (69%) died, 4 (11%) are alive with disease and 7 (19%) alive and well. Concurrent CHT and HPX for NSCLC appears to be feasible, but short-term seem not to be better than in standard treatments.

1106 PUBLICATION

AMIFOSTINE (A), CISPLATIN (C), VINBLASTINE (V): A HIGHLY ACTIVE REGIMEN FOR NON SMALL CELL LUNG CANCER (NSCLC)

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Monthly cycles of A, 740–910 mg/m^2, C, 120 mg/m^2 were given on Day 1 & V, 5 mg/m^2 weekly to 24 Stage IIIA/B & 23 stage IV NSCLC pts. After 2 cycles ACV, Stage III pts received 60 Gy chest RT. 67% stage III, 65% Stage IV responded to ACV. Median follow-ups for Stage III and IV pts are 31 & 15 mos; 1 year survivals are 53% & 60%, respectively. Median survival for Stage III is 16 mos and for Stage IV is estimated to be 17 mos. The spectrum of toxicities from ACV were similar in Stage III/IV pts. A was given on day 1 to protect from C toxicities. Though transient increases in serum creatinine $\geqslant$2 mg/m^2 were noted, protracted elevations lasting beyond day 28 occurred in only 6% (3/47). 11 stage IV pts received $\geqslant$4 cycles therapy. None sustained $\geqslant$40% reduction from baseline creatinine clearance (CrCl). This is in contrast to other trials using $\geqslant$4 cycles of 100 mg/m^2 C in which 30–45% of the pts sustained $\geqslant$40% decrease in CrCl. Grade 4 neutropenia primarily related to weekly V given without A occurred in 46% of cycles. Toxicities from A were nausea/vomiting & transient hypotension. We conclude that amifostine appears to improve the therapeutic index of CV in NSCLC as evidenced by both high response rates & reduced cumulative renal toxicity. This is being tested in a multicenter randomized trial.

1107 PUBLICATION

PACLITAXEL SINGLE AGENT IN THE FIRST-LINE TREATMENT OF ADVANCED NSCLC

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Taxol has produced the best response rate (21%) to date of all single agents in ECOG trials in NSCLC, with is activity confirmed at M.D. Anderson. In 1/94, we initiated a phase II trial of taxol single agent in patients with stage IIIb/IV NSCLC and no prior radio- and/or chemotherapy. In this trial, paclitaxel was administered over 3 h at a dose of 200 mg/m^2 after premedication with dexamthasone, cimetidine and clemastine. The second and all further cycles were administered in an outpatient setting. Cycles were repeated at 28-day intervals. In this ongoing study, 25 patients—21 men and 4 women—with a median age of 60.4 (range, 42 to 69) have been treated to date. Patient characteristics included ECOG performance status 0–1, stage IIIb 7 and stage IV 18; and a histological diagnosis of squamous cell carcinoma in 15 patients (60%), adenocarcinoma 8 patients (32%), and 2 patients (8%) with poorly differentiated carcinoma. At this time, partial remissions have been noted