882

CONFIRMATORY ACTIVITY OF GEMCITABINE IN NON SMALL CELL LUNG CANCER (NSCLC). Le Chevalier, T; Gottfried, M; Gatzemeier, U; Shepherd, F.A; Weynants, P; Cottier, B; Groen, H.J.M.; Rosso, R; Mattson, K; Cortes-Funes, H; Tonato, M; Voi, M; Institute Gustave Roussy, France; Krankenhaus Grosshansdorf, Germany; Toronto General Hospital, Canada; Clinique Universitaires, U.C.L. de Mont-Godinne, Belgium; Clatterbridge Centre for Oncology, U K ; Academisch Ziekenhuis Groningen, Netherlands; Instituto Nationale per la Ricerca sul Cancro, Italy; Helsinki University Central Hospital, Finland; Hospital 12 de Octubre, Spain; Ospedale Regionale, Italy and Lilly Research Centre, Windlesham, UK.

Gemcitabine is a novel pyrimidine analogue with activity against various solid tumours including NSCLC with reported response rates of >20%. Between January and October 1992, 161 chemo-naive pts with inoperable NSCLC were recruited in 9 countries to confirm the results obtained in earlier phase II trials. The dose of gemcitabine was 1250 mg/m^2 over 30 min. weekly x 3 with one week rest. All pts are evaluable for toxicity and 154 who completed one cycle of therapy and had tumour assessment are evaluable for tumor response: 124 male and 37 female, median age 59 years (range 35 -75). Performance status was 0 in 11%, 1 in 83% and 2 in 6%. Histology was squamous in 43%, adenocarcinoma in 53% and mixed adeno-squamous in 4%. Six percent of the patients were stage IIIa, 30% IIIb and 64% were IV. Doses were reduced in 4% of injections and omitted in another 5% due to toxicity but escalated doses were given in 25% of injections (≤ 20% increase at each course) with a maximum dose given so far of 2,100 mg/m^2. At this time 2 (1%) complete responses and 24 partial responses (16%) have been independently validated by an external review board, giving an overall interim response rate of 17% (95% CI: 12-24%), with additional responses awaiting external review. Overall the drug was well tolerated with WHO grade III and IV neutropenia seen in 5% and 1% of injections respectively, and grade III/IV toxicity for haemoglobin and platelets in <1%. Hepatotoxicity (grade III/IV transaminase elevation) occurred in 2%. WHO grade III/IV non-haematological toxicity with an incidence >1% was nausea and vomiting observed in 4% injections. The results of this study confirm the efficacy and mild toxicity of gemcitabine in the treatment of NSCLC, which together with original mode of action make it an exciting agent for use in combination therapy.

883

MULTIVARIATE ANALYSIS OF THE POST-THERAPEUTIC COMPLICATIONS IN THE TREATMENT OF LUNG CARCINOMAS
Bernier J., Bornet C., Thum P., Pampalonna S., Goldhirsh A.
Department of Radiotherapy, San Giovanni Hospital, CH, Bellinzona.

In most patients with lung carcinomas, treatment now combines multimodal approaches. Treatment morbidity has become a major issue for these patients and the aim of this study is to identifiy prognostic factors significantly associated to pulmonary complications following surgery, radiotherapy and/or chemotherapy.

Material : This retrospective study deals with a series of 112 patients with bronchus carcinoma (SCLC : 60 cases; NSCLC : 52 cases).

Methods : The analysis of pretreatment variables is stratified according to patient caracteristics and tumor pattern. Treatment-related variables encompass the type of treatment modality, radiotherapy dose, volume and fractionation. Acute pneumonitis and late fibrosis are the main endpoints of the univariate and multivariate analysis (Cox regression Model).

Results : 1. The most significant prognosticators for acute pneumonitis are the use of multimodal therapeutic approaches and radiotherapy volume. 2. The correlation between high grade clinical symptoms and severe radiological complications is poor. 3. The severity of acute pneumonitis is an excellent pronosticator of late pulmonary fibrosis. 4. The multivariate analysis identifies age, severe anamnestic bronchopathy and irradiation volume as independent prognostic factors for pulmonary fibrosis.

These factors should be carefully assessed in the decision-making process to reduce the incidence of serious pulmonary complications and improve the quality of life of patients with favorable tumor response to treatment.

KEY WORDS : Radiotherapy, Non Small Cell Lung Carcinoma, Small Cell Lung Carcinoma.

884

HUMAN LUNG CANCER: ALTERATIONS OF PARENCHYMAL α1-ADRENERGIC RECEPTORS
Kondratenko T., Zakharova I., Kuzina N.
Research Center of Molecular Diagnostics and Therapy, Moscow, Russia

The adrenergic part of the autonomic nervous system is involved in the pathogenesis of lung diseases, however, this was not investigated in lung cancer. In this study α1-adrenergic receptors have been invesitgated in human lung parenchyma, obtained at the resection of tuberculoma patients within the normal tissues limits and the resection of adenocarcinoma patients. The Scatchard analysis indicated in that α1-adrenergic sites markedly increased in the cancer lung-membrane preparation (control-Bmax=270+/-85fmol/mg; cancer-Bmax=1049+/-117fmol/mg), including membranes of alveoli, bronchioli as well as blood vessels. The increase of α1-adrenoceptors activity may lead to a strong vascular smooth muscle contraction in lung cancer parenchyma and may result in a prevention of metastasis from a primary growth. The advanced observations suggest cancer-induced enhancement in parenchymal α1-adrenergic activity, involving in the regulation of metastasis.

885

CRYODESTRUCTION. CISPLATIN AND INTERFERON ALPHA-2b (INF-2b) FOR CONTROL OF MALIGNANT PLEURA MESOTHELIOMAS (MM)
Zakharychev V., Ganul A. Dep. of Uncology Kiev Institute for Medical Updating
Treatment of MM with cytotoxic drugs and surgery has been dissapointing. We initiated a new approach in this problem. Treatment 11pts with stageII MM included intraoperative cryodestruction of visual tumor in twice "freezing-melting"regime; intrapleural infusion 5 min IU INF-2b on 3-d day after surgery every other day(50-60 min IU in sum); intrapleural infusion Cisplatin 50 mg/m2 on days 7,14,21 (A). Infusions has been repeated every 4 weeks. 3 pts have undergone an adequate surgical removal of MM + 5-FU 15mg/kg by intrapleural infusion to 7,0g in sum(B). Palliative pleurectomy with resection of lung, diaphragm, pericardium in combine with intrapleural 5-FU 8,0 g in sum was performed in 12 pts(C). Median survival was 13,5 mon in A, 14 mon in B, and 10 mon in C. All patients in A are just alive. Treatment toxity was tolerable in all regimens and more postoperative complications were determined in B and C. We conclude that cryodestruction in combine with INF-2b and Cisplatin are an effective agents for MM.

886

HIGH DOSE RATE BRACHYTHERAPY FOR MALIGNANT ENDOBRONCHIAL TUMORS. Hayes, J.L., Lo, T.C.M., Girshovich L., Mower, H.W., and Beamis, J.F., Lahey Clinic, Burlington, MA
We are reporting results of the initial 25 patients treated on our new GammaMed 12i HDR Brachytherapy unit for malignant endobronchial obstruction. There were 68 procedures. Our protocol consisted of 3 weekly sessions of 7 Gy each calculated at a 1 cm radius. Seventeen male patients and 8 female patients were treated, and the median age was 67 years. Twenty-three patients had previous external beam irradiation. Two patients were treated for metastatic endobronchial lesions and the rest had recurrent primary bronchogenic carcinoma. Eight patients underwent YAG Laser excision prior to their first treatment. Survival ranged from 0 to 9 months. We encountered no complications. Of the 15 patients who lived long enough and were evaluable for tumor response, subjective or bronchoscopic improvement was found in 12 patients (80%). HDR Brachytherapy is an effective means in palliation for symptomatic malignant endobronchial disease.

887

A RANDOMIZED TRIAL OF MACC CHEMOTHERAPY WITH OR WITHOUT LONIDAMINE IN ADVANCED NON-SMALL CELL LUNG CANCER. G.F. Buccheri, D. Ferrigno, A. Rosso. Pulmonary divisions, the A. Carle Hospital, Cuneo, Italy.

Lonidamine (LND) is a new drug with an innovative mechanism of action, which could potentiate the activity of some anticancer compounds, without increasing their toxicity. The MACC regimen is scarcely active, but fairly well tolerated, and capable of prolonging the survival of treated patients. Three drugs of this combination (i.e., ADM, CTX, and CCNU) were shown in vitro to be potentiated by the addition of LND. We report a phase III study of 151 patients with advanced NSCLC, randomized to either: arm 1) the MACC regimen as originally described (JAMA 1977,237:2392) -76 pts-, or arm 2) MACC plus LND 150 mg orally t.i.d.-75 pts-. Five of 64 evaluable pts (arm 1) and 9 of 58 (arm 2) had a major tumor response (only 1 complete response was observed in arm 1). Median survivals were 27 weeks (95% CLs, 22 to 34) and 30 weeks (CLs, 23-40) for arm 1 and 2, respectively (p=NS). In both arms toxicity was similar and as expected by the use of MACC. It was mainly gastrointestinal (52% of the patients), and hematologic (anemia, 38%; leukopenia, 24%; thrombocytopenia, 8%), oral (18%), renal (10%), and cardiac (7%). Uncommon side-effects, seen only in pts on LND, were mild to moderate and reversible. We believe that the present findings do not justify further phase III study of chemotherapy with or without LND.