and 36%; median PS 1, 1 and 0. There were 2 toxic deaths, 12 treatment withdrawal (3 MVP, 6 PIN and 3 CaN) and 16 dose- or schedule-modification because of toxicity (6 MVP, 6 PIN 4 CaN). Grade 3–4 leukopenia occurred in 13.4%, 32.4% and 16.2%; grade 3–4; thrombocytopenia in 6.6%, 8.1% and 6.5% and grade 3 anaemia in 3.5%, 1.5% and 3.2% respectively. 6(MVP), 7(PIN) and 4(CaN) objective responses were independently validated. In conclusion both experimental navelbine-containing regimens under investigation are active and feasible in the treatment of advanced stage NSCLC.

1060 POSTER

CLINICAL APPLICATION OF POSITRON EMISSION TOMOGRAPHY FOR STAGING OF THORACIC LYMPHNODES

H. Bischoff, M.V. Knopp[1], C. Manegold, J. Doll[1], P. Drings, G. van Kaick[1]
Thoraxklinik Heidelberg-Rohrbach, Heidelberg
[1]Deutsches Krebsforschungszentrum, Heidelberg, Germany

Positron emission tomography (PET) is a new imaging modality which allows metabolic dependent visualisation of lesions. Due to the intense uptake of F-1 8 deoxyglucose (FDG), tumor as well as metastatic lymphnodes can be imaged with high contrast to the surrounding mediastinum and lung parenchyma. 29 patients with malignant thoracic tumors were studied prior to surgical staging. Staging was done according to the UICC and ATS. N-stages were compared among CT, PET and histopathological findings. For PET-classification, quantitative as well as morphologic information was used. Surgical staging was performed as lymph adenectomy (n = 14), exploratory surgery (n = 5), mediastinoscopy (n = 9) and autopsy (n = 1). The histology of the tumor was adeno carcinoma (n = 5), squamous (n = 8), small cell (n = 14), large cell (n = 1) and mixed tumor (n = 1). The resulting N-staging was N0 (n = 5), N1 (n = 1), N2 (n = 10), N3 (n = 11). The PET N-staging agreed in 18 patients with CT and disagreed in 11. It increased the N-stage in 5 and decreased it in 6 patients. In 4 patients the N2-stage was decreased to N0. In three patients the N-stage was increased to N3. The N-stage agreed in 27 of 29 patients with the surgical N-stage.

1061 POSTER

CANCER FAMILIARITY HAS NO PRACTICAL MEANING IN LUNG CANCER (LC) MANAGEMENT: RESULTS OF A LARGE PROSPECTIVE STUDY

G. Buccheri, D. Ferrigno
The A. Carle Hospital of Chest Diseases, Cuneo, Italy

Old and consolidated experience indicate that the incidence of cancer is higher in certain families than in others. Cancer familiarity (i.e. number and type of cancers occurred in first degree relatives) was prospectively recorded from a series of 548 consecutive patients with a new primary LC. Other variables (in all, more than one hundred) included data from personal life style, clinical history, physical examination, laboratory evaluation, plus radiologic and pathologic tumor findings, and the subsequent clinical course. A second, third, and fourth case of LC within one family was declared by, respectively, 38, 3, and 1 patient; 125 and 32 others had (or had had) one or two relatives with a non-pulmonary cancer. In all, 190 (35% of the sample) had cancer familiarity. But one, no statistically significant difference (based on the χ-square and other nonparametric tests, such as the log rank test for survival differences) was observed between patients with or without cancer familiarity. Female patients showed a higher propeness to have other cancer-affected relatives than their male counter party ($P = 0.028$). The sex-related difference could be related to the lower tobacco, environmental, and professional carcinogenic exposure of females, which makes more important the role of endogenous factors. However, from the practical point of view of managing LC patients, cancer familiarity has no clinical value.

1062 POSTER

EVALUATION OF THE 4TH EDITION OF THE TNM CLASSIFICATION FOR LUNG CANCER AND PROPOSALS FOR THE 5TH EDITION

H. Bülzebruck, M. Schrenk, B. Danzer, M. Odemer, S. Krieger, S. Schäffler, P. Drings, I. Vogt-Moykopf
Departments of Med. Informatics and Biostatistics, Oncology and Thoracic Surgery, Thoraxklinik Heidelberg, D-69126 Heidelberg, Germany

The 4th edition of the TNM classification of lung cancer was presented in 1987. In 1992 a first revision and in 1993 a supplement containing recommendations fort the uniform use were published. The data of 5,333 patients were analysed prospectively to examine the prognostic impact of the recent TNM definitions and to make proposals for a 5th edition, planned in 1997.

The categories of the primary tumor (T) as well as the categories of lymph node involvement (N) satisfied all requirements for a prognosis-relevant classification. M1 should be subdivided into M1a for distant metastasis limited to the contralateral lung and into M1b for other distant metastasis ($P = 0.003$). Stage I should be subdivided into substages Ia for T1N0M0 and Ib for T2N0M0 ($P < 0.001$).

For stage III three substages could be recommended (IIIa: T3N0-1M0, IIIb: T4N0-1M0 and T1-2N2M0, IIIc: T3-4N2M0 and T1-4N3M0), P (IIIa vs. IIIb): <0.001, P (IIIb vs. IIIc): <0.001).

1063 POSTER

THE EFFECT OF CONTINUING SMOKING ON LATE RELAPSES AND SECOND PRIMARY CANCERS IN LONG-TERM SURVIVORS WITH SMALL-CELL LUNG CANCER (SCLC).

See page 22.

1064 POSTER

GEMCITABINE-CISPLATIN COMBINATION IN NON-SMALL CELL LUNG CANCER (NSCLC). A PHASE II STUDY

L. Crinò, G. Seagliotti, M. Marangolo, F. Figoli, M. Clerici, F. De Marinis, F. Salvati, G. Cruciani, L. Dogliotti, G. Cocconi, A. Paccagnella, V. Adamo, P. Incoronato, L. Scarcella, A.M. Mosconi, M. Tonato
Italian Lung Cancer Group

The clinical efficacy and safety profile of a gemcitabine-cisplatin combination was investigated in a 12-centre phase II trial. 48 consecutive previously untreated NSCLC patients were entered. Median age was 60 years (range 37–70); performance status 0–1; 21 patients had locally advanced unresectable stage IIIb disease and 27 disseminated stage IV disease. Gemcitabine 1000 mg/m^2 was administered weekly (days 1, 8, 15) followed by one week rest and cisplatin 100 mg/m^2 monthly (day 2) of each 28-day cycle. This schedule was chosen because of experimental and clinical evidence of synergy when the 2 drugs are given in close sequence, and to assess separately acute side effects. Forty-six patients were evaluable for response and toxicity ($\geq$1 measurable lesion and $\geq$2 cycles). 1 complete response and 26 partial responses were observed for an overall response rate of 58% (95% CI 44–72%), 11 stage IIIb (52%, CI 31–73%) and 16 in stage IV (59%, CI 41–77%). Thrombocytopenia was the main side effect with 51% grade 3–4 toxicity, usually short-lived and responsible for the omission of gemcitabine administration on day 15 in 90 courses of chemotherapy, and no serious bleeding episodes. Non-haematological toxicity was usually mild with one acute but reversible renal failure. The combination of gemcitabine and cisplatin induced a significant response rate both in stage IIIb and IV NSCLC with modest side effects. The regimen deserves further careful evaluation in a phase III prospective randomized trial.

1065 POSTER

RESULTS OF A MULTIMODALITY PREOPERATIVE INDUCTION TREATMENT PROGRAM IN LOCALLY ADVANCED (LAD) NSCLC STAGES IIIA AND IIIB

W. Eberhardt, H. Wilke, G. Stamatis, M. Stuschke, H. Menker, M.R. Müller, M. Stahl, U. Fuths, U. Klaassen, L. Schlenger, A. Haarstrick, V. Budach, M.R. Nowrousian, D. Greshuchna, N. Konietzko, S. Seeber
Department Int. Med. (Cancer Res.), Essen University Medical School, Hufelandstraße 55, 45122 Essen, Germany

Since 3/91, 97 patients (pts) with LAD-NSCLC (mediastinoscopy obligatory) have been entered. Treatment consisted of 3 cycles cisplatin (P) (60 mg/m^2 d 1+7) and etoposide (E) (150 mg/m^2 d 3, 4, 5), q d 22 followed by one cycle simultaneously RTx/CTx (45 Gy, 1.5 Gy twice daily within 3 weeks; P 50 mg/m^2 d 2+9 of RTx, E 100 mg/m^2 d 4,5,6 of RTx) followed by remediastinoscopy and operation. 88 pts are currently off treatment.

Their characteristics: m/f 70/18; median age 55 (30–70); med. PS 1 (0–2): IIIa (more than 1 mediastinal lymph node station involved) 48, IIIb 40. *Results:* (n = 88 pts):

Stage	n	cOR n(%)	OP %	RO %	pCR	MST	3YSR
IIIA	48	29 (60)	33 (69)	29 (60)	13 (27)	18 mts	30%
IIIB	40	25 (63)	26 (65)	18 (45)	9 (23)	20 mts	37%
All pts	88	54 (61)	59 (67)	47 (53)	22 (25)	20 mts	33%

Median observation time of all pts alive 17 months (6–46) (mts). MST in RO-res pts: 32 mts; 14/47 NED/RO-res pts have relapsed so far (5 CNS, 2 liver, 2 bone, 1 pumonal (hematogen), 4 local). 29 Pts who could not be operated: Treatment not completed (medical reasons) 7, PD during CTx ± RTx 7; CTx/RTx refused 4; OP refused 2; irresectable after CTx/RTx 9. *Toxicity:* CTx: leucopenia 3° 32% 4° 8%, thrombocytopenia 3° 17% 4° 11%; infections 3°/4° 4%, 2 early deaths due to septicemia; CTx/RTx: leucopenia 3° 38% 4° 9%, thrombocytopenia 3° 18% 4° 5%, infections 3°/4° 3%, esophagitis 3° 41% 4° 4%; Perioperative: 4 postoperative deaths (1 card. failure, 2 stump insuff, 1 pleural empyema). *Conclusions:* This intensive preoperative treatment program is tolerable and highly effective for these unfavourable prognostic subgroups of LAD NSCLC patients.

1066 POSTER

SURGICAL MANAGEMENT OF NON SMALL CELL LUNG CANCER WITH INVASION OF THE CHEST WALL

F. Fumagalli, R. Cappelli, T. Panigalli, M. Mezzetti

Department of Thoracic Surgery, European Institute of Oncology 20141 Milan, Italy

The chest wall is involved by direct lung tumour extension in approximately 2–8% of the patients. Between 1976 and 1989, 1365 patients underwent resection of non small cell lung cancer and this study is concerned with 73 of these patients (5.3%) who required resection of an area of the chest wall including one or more ribs because of direct tumour invasion (T3).

The overall 5-year survival rate was 31.5% (23 patients); 17 (74%) were N0, 5 (21.7%) were N1 and only 1 (4.3%) was N2.

Our experience confirms earlier reports: stage IIIA patients T3N0M0 have a better 5-year survival rate than N1 and N2, indicating a potentially radical tumour excision even in this stage.

1067 POSTER

DNA CONTENT IN CORRELATION WITH POSTSURGICAL STAGE IN NON-SMALL CELL LUNG CANCER

H.-S. Hofmann, H. Neef, J. Knolle[1], E. Beckhausen, U. Beyer, T. Klapperstück[2], C. Lautenschläger, H.R. Zerkowski

Division of Cardio-Thoracic Surgery

[1]Institute of Pathology

[2]Institute of Dermatology, Martin-Luther-University, 06097 Halle, Germany

The relationship between DNA content and TNM stage, histology, histological differentiation, survival as well as recurrence was assessed in a study of 215 patients with non-small cell lung cancer (NSCLC) who had undergone complete resection (R0).

Cellular DNA content was obtained by image cytometry on paraffin-embedded-tumor tissue and by flow cytometry on tumor cell suspension. DNA aneuploidy was measured in 179 (83%) out of the 215 NSCLC. The aneuploid/diploid ratio were identical in TNM stage, histology and grading. Only in adenosquamous carcionomas the proportion of DNA aneuploid tumors was significantly higher. Aneuploid tumors showed higher recurrence rates (23.2%) during follow-up as diploid tumors (11%). Survival analysis showed that life expectancy of patients with diploid tumors was longer than those with aneuploid carcinomas (5-year survival rate of 69% vs. 49%). The most significant difference was found in patients with adenocarcinoma (5-year survival rate of 100% for diploid tumors vs. 45% for aneuploid tumors).

These results suggest that DNA aneuploidy may provide an independent prognostic factor for patients with NSCLC.

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1068 POSTER

CISPLATIN 120 MG/M^2 VS. CARBOPLATIN 500 MG/M^2 IN COMBINATION WITH MITOMYCIN C AND VINDESIN; A RANDOMIZED PHASE III STUDY IN 164 PATIENTS WITH STAGE IIIB AND IV SQUAMOUS-CELL BRONHOGENIC CARCINOMA

S. Jelić, L. Mitrović, D. Radosavljević, E. Elezar, V. Kovčin, Z. Ristović, S. Kovačević, S. Radulović

Institut za onkologiju i radiologiju, 11000 Belgrade, Yugoslavia

A randomized phase III study of Cisplatin vs. Carboplatin in 1:4 ration in patients with stage IIIb and IV squamous cell bronhogenic carcinoma, in combination with Mitomycin C and Vindesin was performed in 164 patients. The study is still open and accrual of new patients is planed to be stopped by July 1995. The arm A received Cisplatin 120 mg/m^2, Mitomycin C 8 mg/m^2 and Vindesine 3 mg/m^2. The arm B received Carboplatin 500 mg/m^2 with the same dosage of Mitomycin C and Vindesine per cycle. Chemotherapy was applied until signs of progressive disease, 6 cycles at most. Both arms were well balanced regarding age, sex, clinical stage, histological grade and performance status. 84 patients were randomized to the Cisplatin group (83 evaluable for activity) and 80 to the Carboplatin group (76 evaluable for activity). In the Cisplatin group there were 2.41% CR, 30.12% PR, 43.37% SD, 24.10% PD, RR 32.53%, mean time to progression 4.21 ± 3.09 months, median 3.43; mean overall survival 6.72 ± 3.69 months, median 6. In the Carboplatin group there were 5.26 CR, 30.26% PR, 43.24% SD, 21.05% PD, RR 35.72%; mean time to progression 5.01 ± 3.27 months, median 4.40; mean overall survival 7.65 ± 5.26 months, median 6. The Carboplatin arm displayed a higher incidence of grade III/IV hematological toxicity, while the Cisplatin regimen was more emetogenic and nephrotoxic. Carboplatin substituting Cisplatin in the regimen seems to be associated with a similar activity and a longer interval to progression not affecting the overall survival.

1069 POSTER

A STUDY ON THE RELATIONSHIP BETWEEN P53 MUTATION AND SMOKING CIGARETTES FOR HUMAN NON SMALL CELL LUNG CANCER

Li Jinhan, Bi Xiangjun, Peng Zaohui

Department of Oncology, Nanfang Hospital, First Military Medical University, Guangzhou 510515, P.R. China

Recently, to explore the relationship between p53 mutation and smoking cigarettes for human non small cell lung cancer (NSCLC), during the period from 1993 to 1994, the p53 mutation of 52 patients with pathologically proven NSCLC was assessed. In this group, male 43, female 9, the ratio of male to female is 4.8:1. Age incidence from 30 to 71 year-old, median age is 55. The histopathologic categories of 52 cases consisted of 30 patients with squamous cell lung cancer and 22 patients with adenocarcinoma of the lung. ABC technique of immunohistochemistry was used for detecting accumulation of p53 protein of all resected NSCLC specimens. Of them, a mutated allele of one case with adenocarcinoma on bases of detection of p53 mutation with PCR-SSCP analysis was isolated and reamplified. Nucleotide sequence analysis was detected, the result revealed that 280 code AGA has been replaced by ACA. In 25 patients with p53 mutation, the smoking individuals accounted only for 17 cases (68%). In 27 patients without p53 mutation, the smoking individuals accounted for 20 cases (74%). No significant difference was found in both groups statistically ($P > 0.05$). The positive rate of p53 mutation of smoker in the squamous cell carcinoma and adenocarcinoma was 45.5% and 46.6% respectively, there were no significant differences ($P > 0.05$) between the squamous cancer and adenocarcinoma. The results revealed that p53 gene mutation might not be closely related with smoking cigarettes.

1070 POSTER

PHASE II TRIAL WITH DOCETAXEL IN PATIENTS (PTS) WITH NON SMALL CELL LUNG CANCER (NSCLC)

J. Latreille[1], F. Laberge, J. Viallet, A. Maksymiuk, F. Shepherd, K. Gelmon, F. Delorme

[1]Hôtel-Dieu de Montréal, Montréal, Canada

This study proposes to evaluate Docetaxel's activity in pts with advanced and/or metastatic NSCLC. Pts eligibility included no prior therapy measurable disease, Karnofsky performance status ≥60, adequate bone marrow, hepatic, and renal function and a signed informed consent. Treatment (Rx) consisted of Docetaxel 100 mg/m^2 given by IV infusion over one hour every three weeks with Dexamethasone 8 mg PO BID × 5 days starting the day prior to Rx and Diphenhydramine 50 mg IV 30 min. prior to Rx to prevent hypersensitivity reactions. Of the 45 pts entered, 38 have been completed Rx. All are eligible and 32 were evaluable. Of the 6 non evaluable pts, 3 had serious adverse effects, 2 an increase in symptoms and one never got treated. A total of 146 Rx were given. Toxic events included mild to severe hypersensitivity reaction and febrile and non febrile neutropenia. Two deaths were related to febrile neutropenia. One complete and 8 Partial responses were observed in 32 pts (28%). In conclusion, these preliminary results indicate that Docetaxel will probably be an active agent in the treatment of NSCLC.

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