1077 POSTER

PROSPECTIVE ASSESSMENT OF CANCER INCIDENCE AND ANTIPYRINE METABOLISM

E. Radzikowska, K. Onish, E. Chojak
Institute of Tuberculosis and Chest Diseases, Warsaw, Poland

Our previous studies revealed faster metabolism of antipyrine among lung cancer patients and their first degree relatives in comparison with subjects without cancer history in their families.

Among 95 relatives of 27 lung cancer patients and 277 controls cancer morbidity during the period of eight years was analysed.

Forty-two subjects from lung cancer families and 55 subjects from control families had previously assessed antipyrine metabolism.

Two lung cancer cases and 8 non tobacco related cancers were noticed in lung cancer families. In the control group no one developed lung cancer. Also one case of tobacco related cancer and 11 cases of non tobacco related cancers were noticed in controls.

The relatives of lung cancer patients in whom lung cancer was diagnosed had very fast antipyrine metabolism. The possible risk for lung cancer in families of lung cancer patients and connection with antipyrine metabolism were discussed.

1078

RANDOMIZED COMPARISON OF ETOPOSIDE-CISPLATIN VS ETOPOSIDE-CARBOPLATIN AND IRRADIATION IN SMALL CELL LUNG CANCER (SCLC): EVALUATION OF LONG TERM SURVIVAL

see page 22

1079 POSTER

GEMCITABINE PLUS CISPLATIN IN NON-SMALL CELL LUNG CANCER: A PHASE II STUDY

A. Sandler, R. Ansari, J. McClean, W. Fisher, F.A. Dorr, L.H. Einhorn
Hoosier Oncology Group, Walther Cancer Institute, and Lilly Research Laboratories, Indianapolis, Indiana, U.S.A.

In view of the poor current treatment options for metastatic non-small cell lung cancer (NSCLC), there is a clear need for new drugs and combination chemotherapy regimens in this disease. Single-agent gemcitabine has reproducibly produced objective response rates of 20%– 26% in NSCLC in 5 studies worldwide. Cisplatin is a commonly used component of combination chemotherapy regimens in NSCLC. Cisplatin and gemcitabine have been shown to be synergistic in preclinical models. The Hoosier Oncology Group in Indiana conducted a phase II study using gemcitabine combined with cisplatin in metastatic NSCLC. Cisplatin 100 mg/m^2 was administered on day 1 and gemcitabine 1000 mg/m^2 on days 1, 8 and 15 with cycles repeated every 4 weeks up to 6 courses. Thirty patients were entered from February to October 1994, and 26 patients are fully evaluable for toxicity, response and survival. Eligibility requirements included no prior chemotherapy, Karnofsky PS $\geqslant$ 80, measurable disease, and adequate renal, hepatic and bone marrow function. Radiotherapy was permitted at sites other than the measurable lesion(s). Patient characteristics were: 17 male, 9 female; median age, 62 years (range 37–74); median KPS 90. *Histology:* 10 squamous, 10 adenocarcinoma, and 6 large cell. 21 of 26 patients had stage IV and 5 had stage IIIb disease. Eight patients received prior radiotherapy (2 CNS, 1 bone, 5 chest). Toxicity has primarily been haematological, with frequent need to omit doses of gemcitabine on days 8 and/or 15. There were 11 responses in 26 patients for an overall response rate of 42%. This is the highest response rate recorded in a Hoosier Oncology Group NSCLC study. We conclude that cisplatin plus gemcitabine is an active and well-tolerated regimen in advanced NSCLC. We plan to compare this regimen to single-agent cisplatin (100 mg/m^2 every 4 weeks) in a phase III study.

1080 POSTER

PHASE I TRIAL OF GEMCITABINE (GEM) AND CISPLATIN (CP) FOR NON-SMALL CELL LUNG CANCER (NSCLC)

F. Shepherd, Y. Cormier, R. Burges, M. Crump, T. Strack
University of Toronto, Toronto, Canada

This study was undertaken to determine maximum tolerated doses of GEM and CP given weekly ×3 with one week rest. Patients $\leqslant$75 yrs were eligible if they had stage III/IV NSCLC, life expectancy $\geqslant$12 weeks, Hgb $\geqslant$10 g/dl, AGC $\geqslant \times 10^9$/L, platelets $\geqslant 100 \times 10^9$/L, AST and ALT $\leqslant 3 \times$ normal, and creatinine $\leqslant$130 mmol/L. There were 33 male and 17 female pts, median age 62 years (30–75). There were 35 adenocarcinomas, 8 squamous, 6 large cell and 1 mixed tumor. 16 patients were stage III and 34 stage IV tumors. Drug doses, toxicity and response are summarized below:

Dose mg/m^2		No.	Nadir count		ECOG 3/4 toxicity		Response
GEM	CP	of pts	Cycle 1		Cycles 1 to 4		PR/evaluable
			grans	platelets	grans	platelets	
1000	25	7	3.9	151	43/14	14/0	3/7
1000	30	6	2.1	130	33/0	33/17	2/5
1250	30	7	1.6	87	43/29	50/17	0/7
1500	30	7	2.1	142	29/29	67/33	3/7
1750	30	6	1.2	60	33/0	67/17	2/5
2000	30	9	0.7	73	67/33	46/33	2/9
2250	30	8	1.2	60	61/36	57/25	1/7

Response rate was 30% (CI 17–43%), median duration 20 weeks. Dose limiting toxicity in Cycle 1 was not seen at any level, but after Cycle 2, cumulative myelotoxicity necessitated frequent dose reductions at high GEM doses. Thus GEM 1500 and CP 30 will be used for Phase II study. Supported by Eli Lilly, Canada.

1081 POSTER

GEMCITABINE COMBINED WITH CISPLATIN IN NON-SMALL CELL LUNG CANCER (NSCLC): A PHASE I/II STUDY

W.P. Steward, D.J. Dunlop, C. Cameron, D.C. Talbot, J.-P. Kleisbauer, P. Thomas, J.C. Guerin, M. Perol, C. Sanson, G. Dabouis, H. Lacroix
Beatson Oncology Centre, Glasgow, U.K.
NCI Clinical Trials Unit, Ontario, Canada
ICRF Clinical Oncology Unit, Oxford, U.K.
Hôpital Rene et Guillaume Laennec, Nantes, France
Hôpital Sainte Marguerite, Marseille, France
Hôpital de la Croix Rousse, Lyon, France

Gemcitabine (GEM), a novel nucleoside analogue, and cisplatin are among the most active single agents in the treatment of NSCLC, producing reproducible response rates of approximately 20%. The two drugs are attractive candidates for combination: dissimilar modes of action with preclinical evidence for potential synergistic tumour cell killing, and largely non-overlapping side-effect profiles. This phase I/II study was designed to determine the maximum tolerated dose of cisplatin in the combination up to a predetermined maximum of 100 mg/m^2, and safety and efficacy. GEM 1000 mg/m^2 was given as a 30 minute iv infusion weekly × 3 repeated every 4 weeks. Cisplatin was given immediately after the 3rd infusion of GEM in each cycle. In the phase I portion of the study cisplatin was escalated from 60 to 75 to 100 mg/m^2 in successive cohorts of 3 patients, using an adaptive control algorithm. Further patients were then accrued into the phase II portion of the study and treated at 100 mg/m^2 cisplatin. Patients treated at 100 mg/m^2 cisplatin in the phase I portion of the study were also evaluable for response. Characteristics of all 66 patients recruited were: males 55, age range 39–74. PS: 0 in 4, 1 in 55, 2 in 7. *Histology:* adenocarcinoma 22, squamous 32, large cell 11, unspecified 1. Stage: IIIa in 2, IIIb in 41, IV in 23. Toxicity was easily managed at 100 mg/m^2 cisplatin (data currently available for 55 patients and 236 courses). The incidence of combined worst WHO grade 3 and 4 toxicities per patient was: neutropenia 51%, thrombocytopenia 25%, ALT/AST 2%, alopecia 2% fever 4%, nausea and vomiting 50%. Neutropenia and thrombocytopenia were both of short duration and uncomplicated. No serious renal toxicity was seen. 52/60 eligible patients were evaluable for response assessment in the phase II portion of the study. 20 PRs were seen, for a response rate of 38%. This combination of gemcitabine and cisplatin is well tolerated with promising activity. Further trials are required to assess whether the schedule used is optimal.

1082 POSTER

ON LINE ELECTRONIC PORTAL IMAGING IN LUNG IRRADIATION: USEFULNESS IN CORRECTION AND DEFINITION OF ANATOMICAL LANDMARKS

J. Van de Steene, F. Van den Heuvel, M. Coghe, D. Verellen, C. Claassens, V. Vinh Hung, G. Storme
Department of Radiotherapy, A.Z.-V.U.B., Brussels, Belgium

We studied the usefulness and feasibility of on line electronic portal imaging (EPI) with intra fractional correction of table position in the irradiation of lung cancer.

Antero-posterior (AP) and oblique anterior (OA) fields of 160 sessions from 8 patients were evaluated before and after correction.

For the AP fields the errors in positioning (longitudinal, lateral and rotational) were measured using the in-house developed OPIDUM system, using lung tops and carina as anatomical landmarks. After correction of the table position the rest of the fraction dose was administered