Results: Increase in doxorubicin intracellular accumulation as well as doxorubicin binding to DNA under genistein action was detected in most tumor samples investigated.

Conclusions: 1) Functional activity of MRP is an index of most NSCLC. 2) Taking into account high frequency of MRP gene or protein expression and high functional activity of MRP revealed in most lung tumors we answer the question proposed above: polymerase chain reaction, immunoblotting and immunohistochemistry analysis should be admitted as adequate methods to determine MRP-phenotype for multidrug resistance prediction in NSCLC patients. Supported by Russian Foundation for Basic Research (No. 01-04-49213)

822 POSTER

Correlation between tumor necrosis factor-alpha and D-dimer levels in non-small cell lung cancer patients

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Background: Recent studies have shown that activation of fibrinolysis occurs in non-small cell lung cancer (NSCLC), although the origin of this activation could not be related to consistent changes in plasminogen activator and inhibitor levels. Neutralization of endogenous tumor necrosis factor-alpha (TNF) in endotoxemia completely prevents fibrinolysis, suggesting a direct role of this cytokine in the activation pathway of the fibrinolytic system. Increased serum TNF levels can be found in lung cancer. Thus the present study was designed to investigate whether a correlation exists between TNF and coagulation (thrombin-antithrombin III, TAT) or fibrinolysis (D-dimer) activation in patients with NSCLC.

Methods: 130 patients with NSCLC (n=65, 53 males, mean age 65±8) or chronic obstructive pulmonary disease (COPD)(n=65, 51 males, mean age 67±9), treated at our Institutions, were enrolled. As control group 65 healthy donors (51 males, mean age 61±14) were studied. NSCLC was histologically diagnosed as adenocarcinoma (n=32) or squamous cancer (n=33), and staged according to the TNM classification: Stage I 29%, Stage II 9%, Stage III 36%, and Stage IV 26%. Plasma TNF (R&D) and TAT (Dade-Behring) levels were determined by ELISA kits. D-dimer levels were measured by an automated analyzer (Roche).

Results: The results obtained showed that median D-dimer levels were higher in NSCLC patients (2.95 ug/ml) compared either to COPD patients (1.07 ug/ml, $p<0.0001$) or controls (0.34 ug/ml, $p<0.0001$). Positive TNF levels (>10 pg/ml) were found in 26% of NSCLC compared to 3% of COPD and 4% of controls ($p<0.0001$). Median TAT levels were elevated in both NSCLC (6.9 ug/L) and COPD (5.7 ug/L) patients compared to controls (1.8 ug/L, $p<0.001$). Correlation analysis showed that D-dimer strongly correlated with TNF (rho=0.35, $p<0.005$), but not TAT levels, in NSCLC patients. Thus, to further analyze the relationship between D-dimer and clinical and laboratory variables of NSCLC, a multiple regression analysis including age, sex, stage, diagnosis, D-dimer, TAT and TNF levels was performed. Final model by stepwise analysis showed that TNF levels (regression coefficient= 0.38, $p<0.03$) were independently related to VEGF, but only in the subset of patients with adenocarcinoma.

Conclusions: These results suggest that increased levels of TNF might be responsible for an activation of fibrinolysis in patients with lung adenocarcinoma. *Partially supported by Grant PF Ministero della Sanità.*

823 POSTER

A full Navelbine Oral (NVB oral) treatment in combination with Cisplatin (P) followed by NVB oral single agent as consolidation therapy in advanced non small-cell lung cancer (NSCLC)

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Background: The combination of alternating NVB iv/oral with P has demonstrated similar activity as a reference regimen NVB iv + P in the treatment of advanced NSCLC (Jassem et al, Ann Oncol 2002). A multinational phase II trial was performed to investigate a new schedule of a full NVB oral treatment in combination with P followed by consolidation therapy with NVB oral as single agent in advanced NSCLC. Patients and methods: chemonaive stage III/IV NSCLC patients (pts) were eligible to be treated with 4 cycles on a 3 weekly schedule combining P: 80 mg/m2 on d1 with NVB oral: 60 mg/m2 on d1 & d8 for the first cycle with dose escalation of NVB oral at 80 mg/m2 on d1 & d8 for the following cycles in absence of grade 3-4 neutropenia. Pts with objective response (OR) or stable disease (SD) received consolidation therapy with weekly NVB oral.

Results: between 04/01 and 04/02, fifty six pts were included (M/F 40/16), median age was 60 years (40-70), median KPS 90% (80%-100%), squamous (43%)/adenocarcinoma (45%), stage IV (70%), IIIB (22%). Fifty-five pts were evaluable for safety and 49 pts for efficacy. A total of 180 cycles of combination therapy were administered with a median of 4 cycles (1-5), the RDI was 86% for NVB oral and 96% for P. As consolidation therapy, 25 pts received a total of 281 administrations of NVB oral with a median of 9 (6-24). Thirteen pts achieved partial response (OR: 26.5%) and 22 pts (44.9%) had stable disease. Median progression free survival and overall survival were 3.8 and 10 months respectively. The main grade 3-4 toxicities (NCI-CTC) were neutropenia 34,5% pts, nausea 5.4% pts, vomiting 8.9% pts, fatigue 12.5% pts, one pt experienced grade 3 neuropathy while another one had grade 3 constipation and two pts developed neutropenic infection.

Conclusion: this schedule of NVB oral + P provides comparable activity as standard regimen with iv form with a better convenience. The consolidation therapy with NVB oral single agent maintained the therapeutic benefit and improved the patient acceptance and comfort.

824 POSTER

Role of gross tumour volume and dose parameters on outcome and toxicity of patients undergoing concurrent chemo-radiotherapy for locally advanced non-small cell lung cancer

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Background. Concurrent chemo-radiotherapy (CRT) is a recommended treatment for locally advanced NSCLC. However, CRT is generally associated with higher frequency of toxicity when compared to radiotherapy alone, and the prognosis still remains poor. The aim of this study was to evaluate the prognostic role of gross tumour volume (GTV) on clinical outcome, regardless of T and N status. In addition, we analysed variables important for the development of lung toxicity.

Materials and methods. We analysed retrospectively data from 25 patients (pts) with locally advanced NSCLC treated at our institution between 1999 and 2001. Pts characteristics were as follows: mean age 59.9 years (range 44-76), PS 0-1, stage IIIA/N2 (6 pts) and IIIB (19 pts), M/F ratio = 16/9. Pts received concurrent CRT, according to the following schedule: weekly paclitaxel 100 mg/m^2 plus carboplatin AUC 2 for 3 weeks, followed by weekly paclitaxel 60 mg/m^2 plus carboplatin AUC 2 for 6 weeks with concomitant conventional thoracic radiotherapy, 2 Gy per fraction, 5 fractions per week up to 60 Gy. Dose volume histograms were collected from the 3-D treatment plans. GTVs were recalculated for all pts and correlated with time to progression (TTP) and overall survival (OS). In correlation with the development of radiation pneumonitis (RP) WHO grade 2 or higher, the following variables were examined: GTV, planning target volume, mean lung dose, V20 and V30 (volume of lung receiving more than 20 and 30 Gy respectively). Lung parameters were considered both for two lungs taken as a paired organ, as for each lung separately.