Taken together, only NSCLC and their derived cell lines were CD97+. The different epitopes of the molecule showed varying distributions within these tumours. SCLC and corresponding cell lines did not express CD97.

156 POSTER

Analysis of MAC-2 binding protein/90k expression in lung cancer

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Purpose: Mac-2 binding protein (Mac-2BP/90K) has been reported to induce the overexpression of MHC and cell-adhesion molecules on cultured tumor cells and to be overproduced in patients with various types of cancer and viral infection. Therefore, this protein is thought to play a crucial role in cellular immune responses in hosts. In this study, we analyzed the expression of Mac-2BP/90K in cultured lung cancer cell lines and tumor tissues from patients with primary lung cancer, and its immunogenicity as a tumor antigen.

Methods: Six lung cancer cell lines and 28 tumor tissues from lung cancer patients were examined for Mac-2BP/90K mRNA expression by Northern hybridization. Sera from cancer patients (n=18) and healthy donors (n=6) were studied for their reactivity to Mac2-BP/90K peptides by ELISA.

Results: Five of 6 (83%) cancer cell lines and 17 of 28 (60.7%) tumor tissues were shown to express high levels of Mac2-BP/90K mRMA. Serum levels of antibodies to Mac-2BP/90K peptides were elevated in 3 of 18 (16.7%) patients but in none of the healthy donors.

Conclusion: Mac-2BP/90K is suggested to be abundantly expressed in lung cancer cells, and to be sufficiently immunogenic to elicit humoral immunity specific for this molecule in cancer patients. Mac-2BP/90K is expected to be useful as a tumor antigen in immunotherapy for lung cancer.

157 POSTER

Neoadjuvant chemotherapy and extrapleural pneumonectomy (EPP) for malignant pleural mesothelioma (MPM)

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Objective: Pilot study to examine the tolerance and outcome of a pre-operative chemotherapy followed by EPP in patients (pts) with potentially resectable MPM.

Patients and Methods: From May 1999 to June 2000, 16 pts were evaluated by an interdisciplinary team for a multimodality therapy consisting of 3 cycles of preoperative chemotherapy with cisplatin (80 mg/m^2 day 1 every 28 days) and gemcitabine (1000 mg/m^2 days 1, 8 and 15), followed by EPP with or without radiation therapy to the area at risk.

Results: The cohort included 1 woman and 15 men with a median age of 57 years (range 48 to 68). Fifteen pts received all 3 cycles of chemotherapy. Major toxicity was haematological. The dose of gemcitabine had to be reduced due to thrombocytopenia in 15 of 47 cycles. Response was evaluated by CT scan. Seven pts had partial remission (43%), 5 no change (31%) and 4 disease progression (25%). Thirteen pts (82%) underwent an EPP. Two pts with progressive disease were not operated on and one pt with no change had only an explorative thoracotomy. Eleven pts had pure epithelial cell type tumors. In one pt the diagnosis of MPM could not be confirmed. Hilar or mediastinal lymph nodes were involved in 3 pts. There was no perioperative mortality. Major perioperative complications included atrial fibrillation (2 pts), acute coronary syndrome (1 pt), chylothorax (2 pts) and bronchial fistula (1 pt). All complications were treated successfully. Ten pts received postoperative radiotherapy. One pt died 7 weeks after EPP from suspected pulmonary embolism. Two pts died from relapse 11 and 19 months after initiation of chemotherapy. Four pts are alive with relapse occurring 9, 13, 15 and 18 months after start of treatment. Six pts are alive without evidence of recurrent disease. At one year, overall and event-free survival is 72% and 65%, respectively. The median survival and event-free survival is 19.4 and 15.4 months, respectively. Up dated results will be compared to our previous series of surgery, followed by chemotherapy and radiotherapy.

Conclusion: Chemotherapy with cisplatin and gemcitabine is effective in earlier stages of MPM. EPP after preoperative chemotherapy is feasible in the hand of an experienced surgeon. Treatment related complications in the perioperative period are manageable. Toxicity is acceptable and is comparable with our results of the trimodality therapy with postoperative chemotherapy. Based on this result we initiated a multicenter phase II study within the SAKK focusing on quality of life issues.

158 POSTER

A prospective infection survey in patients with lung cancer admitted to a cancer hospital

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Purpose: To delineate more precisely the nature and sources of infection in lung cancer patients.

Methods: All patients with lung cancer admitted into a cancer university hospital and developing any infection were included in a prospective survey. Characteristics of the patients, type and source of infection, antibiotherapy and outcome were registered.

Results: 277 patients developed 440 infectious episodes between January 1997 and January 2001. Bacteremia occurred in 8.2% of the cases; Gram positive bacteria, mainly staphylococci and streptococci, accounted for the majority of the documented pathogens (70.7%). The majority of the documented infections originated from the lung (55.5%). They consisted mainly in bronchitis (55.3%) and pneumonia (38.9%). The most frequent pathogens isolated from the airways were Haemophilus influenzae (34.8%), Streptococcus pneumoniae (10.9%), Staphylococcus aureus (8.5%), Moraxella catarrhalis (7.5%) and Pseudomonas aeruginosa (7%). Gram negative bacteria accounted for the majority of documented pulmonary infectious episodes (75.1%). Except for ampicillin resistance in Moraxella catarrhalis (80%), few bacteria were resistant to conventional antibiotherapy.

Conclusion: Our study confirms the importance of lung as a source of infection in lung cancer patients. If needed, empirical antibiotherapy must have adequate activity against Gram positive bacteria

159 POSTER

Combination effects of amrubicin, a novel anthracycline, with cisplatin on human lung cancer cells

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Amrubicin is a novel completely synthetic 9-aminoanthracycline derivative and its C-13 alcohol metabolite, Amrubicinol, inhibits purified human topoisomerase II (topo II). We examined the effect of combination with Amrubicinol and cisplatin (CDDP) in vitro using small cell lung cancer cell line (SBC-3) and adenocarcinoma cell line(Ma-1), using WST assay and analyzed by isobologram. Both drugs used together simultaneously and consequently, the combined effects were additive interaction both simultaneous and sequential administration. A high concentration of CDDP (300 maikuro M) enhanced the topoisomerase II inhibitory activity of Amrubicinol determined by DNA decatenation assay. On the other hand, Amrubicinol increased formation of DNA interstrand cross-links (ICL) on the cells, which analyzed using ethidium bromide binding fluorescence assay when we observed by simultaneous exposure to CDDP (0-30 maikuro M) and Amrubicinol (2 maikuro M) compared with CDDP alone. These biological interactions might result in synergistic interaction between Amrubicinol and CDDP.

160 POSTER

Ifosfamide, mesna and interferon alfa combination therapy in malignant mesothelioma: results of a single center in central Anatolia, Turkey

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Purpose: Malignant mesothelioma (MM) is a serious clinical problem in Central Anatolia due to environmental exposure to asbestos and erionite. MM is an agressive tumor and management is difficult. The purpose of study was to determine the efficacy of ifosfamide, mesna and interferon alfa combination therapy in MM patients.

Methods: The patients with histopathologically confirmed MM received a combinaton of Ifosfamide 3g/m2 1-3 days, uroprotective agent Mesna 3g/m2 1-3 days every 3 weeks and Interferon alfa (IFN) 4.5MU 3 days a week for 6 months as first line chemotherapy.

Results: We enrolled into the study 35 patients with median age 54 years (range 24-75). 18 patients were male, 17 female. 27 patients had malignant pleural mesothelioma, 8 malignant peritoneal mesothelioma. 3 patients were sarcomatous subtype and 2 mix subtype. Remaining patients were pure epithelial subtype. Median 4 cycles (range 1-7) of chemotherapy were administered. Response to chemotherapy was determined in 22 patients who received 2 or more cycles of chemotherapy. There was no complete remission. The partial response rate (PR) was 36.3%. Stable disease was obtained in 36.3% of patients. Estimated overall survival (OS) and progression free survival (PFS) were 12±3.88 (95% CI 4.39-19.61) and 9±3.12 (95% CI 2.88-15.11) months respectively. 2 years survival rate was calculated as 22.0% and 2 years PFS rate 15.7%.

Conclusion: A favourable response rate could be achieved in malignant mesothelioma with ifosfamide, mesna and IFN combinaton therapy.

161 POSTER

Mesothelioma - a new therapeutical approach with Tomudex

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Purpose: Prior experiments showed a missing uptake of *H-thymidine but not of *H-thymidinemonophosphate into the nucleus of mesothelioma cells and suggested a diminished activity of the enzyme converting thymidine to thymidinmonophosphate, the thymidine kinase.In order to get evidence and to evaluate a new treatment regimen we tested the effects of a drug blocking the activity of the enzyme providing thymidinemonophosphate by de novo synthesis, the thymidylate-synthetase tomudex alone and in in combination with thymidine and thymidinmonophosphate.

Methods: Established cell lines were tested in 96 multi-well plates with Tomudex 1ng/ml versus control without supplements in the culture medium with or without thymidine and thymidinemonophosphate ranging from a dose level 0-400μmol. Cell survival was evaluated by an MTT test.

Results: All tested mesothelioma cell lines, the renal cell carcinoma lines and the ovarian cancer cells were sensible to Tomudex at a dose level of 1ng/ml showing a cell survival of 20%. Thymidine showed toxic effects at a dose level of 100μmol and thymidinemonophosphate in a dose range of 50μmol. The toxic effects caused by tomudex could be completely antagonized in the mesothelioma cells by thymdinemonophosphate 4 μmol whereas thymidine antagonized about 80% at a dose level of 30-40μmol/ml. In the renal cell carcinoma cell lines and in ovarian cancer cells complete antagonism of tomudex effects was achieved with thymidine and thymidinemonophosphate 4 μmol.

Conclusion: Tomudex provides a therapeutical approach to mesothelioma. Antagonism of toxic effects caused by tomudex can be taken as a measure for thymidine kinase substrate affinity in the mesothelioma cells. The results suggests a low substrate affinity providing a possibility of preventing side effects without altering the therapeutical effect.

162 POSTER

Evaluation of response to chemotherapy in lung cancer patients: an interdisciplinary comparison using RECIST and WHO criteria (ATOM 004)

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Imaging based assessment of objective response of a tumor to an anticancer treatment is a critical issue in cancer patient management both in daily practice and in clinical trials. Still, a precise and reproducible assessment of the tumor size is usually difficult. In fact, the evaluation criteria, the technique used, and the observer's background and experience may affect the evaluation result. In this study, we evaluated different specialists dealing with assessment of response to chemotherapy. In particular, we addressed the impact of the observer's background and experience, and the technique used on the accuracy of the tumor measurement; the consistency of measures by WHO vs. RECIST criteria is also reported.

Briefly, 25 medical doctors and 5 medical students were asked to measure a set of 11 selected tumor images on serial chest CT scans from NSCLC patients treated with chemotherapy. In order to represent the different specialists actually involved in lung cancer patient management, the M.D. population included 5 radiologists, 5 thoracic surgeons, 5 radiation oncologists, 5 pulmonologists, and 5 medical oncologists from the staff of the local Hospital and the local Faculty of Medicine. The years since M.D. degree varied widely among the physicians, ranging from 3 to 33 years, as well as the observer's familiarity with tumor measurements. The observers were asked to identify 1) the longest diameter (RECIST, unidimensional evaluation), and 2) the longest diameter and its perpendicular diameter (WHO, bidimensional). The technique of measurement (i.e. ruler, paper, compasses) was left up to the observer. Four lesions were also evaluated using the loop of the tumorimeter. The measurements by the radiologists were used as reference values.

A preliminary comparison of RECIST and WHO criteria shows consistent overall response rates (correlation coefficient 0.79). In addition, there is no significant difference in the accuracy of measurements among the different disciplinary groups (p =0.0914, C.I. 95%). However, medical oncologists gave the most accurate evaluations. Familiarity with measuring tumor lesions as well as years since MD degree do not seem to correlate with the measurement accuracy.

163 POSTER

Resection of pulmonary nodules equal or less than 10mm in diameter by video-assisted thoracic surgery with CT-guided hook wire technique

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The aim of this study was to assess the experience with video-assisted thoracic surgery for the resection of small pulmonary nodules (equal or less than 10 mm in diameter).

This study included 27 patients. The mean age of the patients (14 men, 13 women) was 59 years (range, 44 to 74years). All nodules were detected by computed tomography but not by routine chest radiography. All nodules were located at a maximum of 3 cm from the visceral pleura. The injection of hook wire with the guide of computed tomography was done about 90 minutes before operation.

Video-assisted thoracic surgery was converted into thoracotomy in 6 patients, because of diffuse pleural adhesion in 5, inability to confirm localization of nodule due to dislocation of the hook in 1. The mean diameter of resected nodules was 6.9 mm (range, 4 to 10 mm). All patients underwent wide wedge resection of lung with endoscopic devices. The nodule was malignant lesion in 10 patients (37%) and benign in 17 patients (63%). The malignant lesions included primary lung adenocarcinoma in 8 and metastatic tumor in 2. Benign lesions included inflammatory fibrous nodule in 9, intrapulmonary lymphnode in 5, inflammatory pseudotumor in 1, anthoracosis in1, sarcoidosis in1. In 8 primary lung cancer patients, wide wedge resection was a final procedure in 6 with bronchioloalveolar carcinoma, right basal segmentectomy in 1 and right middle lobectomy in 1. There was no mortality and no pulmonary complication. The mean duration of postoperative drainage was 3.6 day (range, 1 to 7).

We concluded that resection of pulmonary nodule equal or less than 10mm in diameter by video-assisted thoracic surgery with CT-guided hook wire technique was seemed to be feasible.

Non-small cell lung cancer

164 POSTER

Cooperative role of telomerase activity and p16 expression in the prognosis of non-small cell lung cancer

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Telomerase activity and p16 expression can be considered as two of the most important molecular markers implicated in tumorigenesis. Our main aim was to study the cooperative role of both molecular alterations in the prognosis of patients surgically resected for non-small cell lung tumours.