

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 combination therapy.

161

POSTER

Mesothelioma - a new therapeutical approach with Tomudex

G. Zopf¹, G. Kovacs¹, K.H. Berghäuser², G. Seibold², H. van Lieven¹.

¹ Zentrum für Radiologie der Justus-Liebig-Universität Gießen, Wilhelm-Conrad-Röntgen-Klinik, Abteilung Strahlentherapie, Gießen, Germany; ² Strahlentherapie der Justus-Liebig-Universität Gießen, Zentrale Biotechnische Betriebseinheit, Gießen, Germany;

³ Thüringen-Klinik Saalfeld, Pathologisches Institut, Saalfeld, Germany

Purpose: Prior experiments showed a missing uptake of ³H-thymidine but not of ³H-thymidinemonophosphate into the nucleus of mesothelioma cells and suggested a diminished activity of the enzyme converting thymidine to thymidinemonophosphate, 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 combination with thymidine and thymidinemonophosphate.

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 thymidinemonophosphate 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 suggest 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)

O. Belvedere^{1,2}, F. Grossi^{1,2}, S. Meduri^{1,3}, T. Ceschia¹, G. Fasola^{1,2}, A. Morelli^{1,4}, C. Sacco^{1,2}, A. Sibau^{1,2}, G. Talmassons^{1,5}, A. Sobrero^{1,2}.

¹ Alpe-Adria Thoracic Oncology Multidisciplinary Group, Udine, Italy; ² PUGD-AOSMM, Medical Oncology, Udine, Italy; ³ AOSMM, Radiology, Udine, Italy; ⁴ AOSMM, Thoracic Surgery, Udine, Italy; ⁵ AOSMM, Pulmonology, Udine, Italy

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

H. Yoon¹, T. Yana², K. Iwase³, J. Higaki³, M. Takada², W. Kamiike³.

¹ Rinku General Medical Center, Thoracic Surgery, Izumisano, Japan;

² Rinku General Medical Center, Respiratory Medicine, Izumisano, Japan;

³ Rinku General Medical Center, Surgery, Izumisano, Japan

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 74 years). 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, anthracosis in 1, sarcoidosis in 1. 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

P. Iniesta¹, R. Gonzalez-Quevedo¹, A. Moran¹, C. De Juan¹, A. Sanchez-Pernaute², A. Torres², E. Diaz-Rubio³, J.L. Balibrea², M. Benito¹. ¹ Faculty Of Pharmacy, Complutense University, Biochemistry And Molecular Biology, Madrid, Spain; ² San Carlos Hospital, Surgery Service, Madrid, Spain; ³ San Carlos Hospital, Oncology Service, Madrid, Spain

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.