1258 ORAL

PRONOSTIC VALUE OF CYFRA 21.1 VARIATION IN LUNG CANCER

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We have investigated the usefulness of CYFRA 21-1 as indicator of therapy effectiveness and prognostic in lung cancer. Forty-two patients with primary lung cancer were selected on the basis of a high CYFRA 21-1 serum level (> 3.3 ng/ml) on diagnosis time. All cases were histologically proven: 6 small cell carcinomas, 17 squamous cell, 11 adenocarcinomas and 8 undifferentiated. Serial monitoring of CYFRA 21 was performed during modalities of first therapy (chemotherapy 36, irradiation 3, surgery 3 cases). The serial values were analysed according to response to treatment and overall survival. Thirty five of 42 patients had a significant decrease (SDS) (> 50% or return to normal) of CYFRA 21 serum level and 27 returned to normal values (NV). Twenty-two (62%) of SDS patients, and 18 of NV patients (66%) had a clinical response to therapy, making CYFRA 21 a moderate indicator in terms of specificity. Clinical response, however, was always associated with a SDS of CYFRA 21. Eleven clinical relapses were observed, that were reflected by a positive CYFRA 21 in 8 (72%) cases at the time of radiological or clinical relapse. In three patients CYFRA 21 values preceded the clinical detection by one month. Survival data were available for 36 patients. A statistically significant difference ($P = 0.01$) was found in survival depending on return to normal of CYFRA 21 during therapy or not (42 and 27 weeks respectively). Initial CYFRA value was not correlated with survival.

We conclude that serial monitoring of CYFRA 21 serum levels may be a useful prognostic tool of response and longer survival in lung cancer patients.

1259 ORAL

CYFRA 21-1 AND TPS—NEW MARKERS IN LUNG CANCER

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Multiple tumor marker analysis (CYFRA 21-1, TPS and CEA) in Lung Cancer was studied in 212 patients aiming to define specificity and sensitivity as well as treatment efficacy. We used 95% specificity versus benign lung pathology in 74 pts with infectious, non-infectious and obstructive lung diseases. Cut-off values of 2.8 ng/ml, 196 U/L and 4.8 ng/ml for CYFRA 21-1 (CYFRA), TPS and CEA respectively were used. According to histological type of the tumor, the sensitivities were the following:

		Sensitivity (%)		
Lung carcinomas	No Pts	CYFRA	TPS	CEA
a) Adeno (Ad)	37	35.1	32.4	48.6
b) Squamous (Sq)	31	51.2	36.7	35.5
c) Adenosquamous (ASq)	4	75.0	50.0	50.0
d) Undifferentiated	8	25.0	37.5	50.0
e) Small (S)	17	41.2	47.1	52.9
Metastasis to lung	34	41.3	35.3	44.1
Pleural mesothelioma (PM)	7	42.9	42.9	0

For Sq and ASq CYFRA was the leading marker compared to TPS and CEA. Increased sensitivity for Ad, Sq and S was obtained by the combined determination of the markers CYFRA, TPS and CEA up to 67.6%, 70.9% and 76.5%, respectively. TPS and CYFRA showed a high sensitivity for PM while CEA showed no sensitivity at all. A high correlation between CYFRA and TPS (r = 0.7) was found for all types of lung cancer. Serial measurements of these markers were useful in determining the effect of therapy or recurrence of disease. This study indicates the clinical relevance of tumor marker panels for lung cancer.

1260 ORAL

ASSAYING LACTATE DEHYDROGENASE (LDH) IN LUNG CANCER (LC): RESULTS FROM A LARGE PROSPECTIVE STUDY

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Six of the 23 original investigations considered in a recent review on prognostic factors (Buccheri *et al.*, *Eur Respir J* 1994, 7, 1350–1364) did not find that LDH was prognostically relevant. LDH was prospectively recorded from a series of 479 consecutive patients with a new primary LC. Other variables recorded (more than 100) included anthropometric, clinical, physical, laboratory, radiological, and pathologic tumour findings, as well as the subsequent clinical course. The serum levels of LDH did not significantly change according to sex, age, tumour cell type, and a number of other different variables. On the contrary, they were significantly related with the following factors:

Variable	W. loss	KPS	WBC	ALPH	GOT	GPT	CEA	TPA	Stage
Sr	109	−.243	.091	.171	.325	.175	.117	.254	.298

A univariate survival analysis showed that lower values of LDH were strongly associated with a poor prognosis ($P = .00000$ by the log rank test). A multivariate survival analysis (Cox's model) resulted in the following significant predictor variables (in decreasing order of importance): Stage of disease, performance status, weight loss, LDH, sex, TPA, and serum creatinine. LDH is confirmed in this study as a valuable biomarker of tumour extension and clinical evolution in LC. Its possible utility appears to be even superior to that of more 'classic' tumour markers and merits further attention.

1261 ORAL

CLINICAL EVALUATION OF SPECIFIC ASSAYS FOR FREE PSA AND TOTAL PSA

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It is now well known that PSA assays measure simultaneously free PSA (FPSA) and PSA bound to α-1 antichymotrypsin (PSA-ACT). Furthermore specific measurement of the free form gives additional information on PSA in the distinction between benign prostate hypertrophies (BPH) and prostate cancer.

In order to evaluate the contribution of free PSA in addition to that of total PSA, we tested 105 patients' serum with prostate pathology (prostate cancer or BPH). All patients had a digital rectal examination, a total PSA measurement (values between 2 and 30 ng/ml) and possibly a biopsy as well.

Results obtained showed that with the total PSA (cut-off 4 ng/ml), the measurement does not allow a good discrimination between BPH and prostate cancer (specificity of 46%). For this population (105 patients) the positive predictive value (PPV) of total PSA was only 48%.

The use of free PSA measurement and the ratio of free PSA to total PSA (F/T PSA) allowed the PPV to rise to 87%.

These first results showed that for the patient population which had given low specificity for a simple total PSA measurement (4 to 14 ng/ml), the ratio F/T PSA allowed the detection of 60% prostate cancer with a specificity of 95%.

1262 POSTER

CYFRA 21.1: A POTENTIAL MARKER IN MESOTHELIOMA?

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Mesotheliomas are difficult to diagnose and clinical follow-up is often hampered by lack of measurable target lesions. In the majority of cases, growth rate is not well measurable and the effect of experimental, chemotherapeutic regimens cannot easily be measured. Cyfra 21.1 measures fragments of cytokeratin 19 in serum. The assay appears to be a sensitive marker for Non Small Cell Lung Cancer and our results indicate that it is also of use in Mesothelioma. Cyfra 21.1 was measured in 31 patients with a confirmed diagnosis of mesothelioma. Using a normal cut off level of 2.3 ng/ml, 15 patients had a median survival of 13 months and 16 patients with values >2.3 had only a 7 month survival. Comparison of survival curves showed a significant difference between these groups (logrank $P = 0.019$). In a limited number of patients, who were followed prospectively, a correlation between disease and Cyfra 21.1 was observed.

In conclusion, Cyfra 21.1 has a prognostic value and can monitor disease progression.

1263 POSTER

ADVANCED BREAST CANCER (ABC) AND CEA, MCA, CA 15.3: CORRELATION WITH RESPONSE TO TREATMENT

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In this study we evaluated the correlation with serum levels of CEA, MCA and CA 15.3 and response to treatment (tr) in 147 patients (pts)

with ABC. Markers were determined before, during and after tr (hormono or chemotherapy). Cut off was: CEA = 5; MCA = 11; CA 15.3 = 30. Pre-treatment CEA was elevated in 51% of pts, MCA in 72% and CA 15.3 in 71%. In this subgroup of pts these markers were correlated to response to tr respectively: CEA in 75% of pts, MCA in 82% and CA 15.3 in 79%. We observed that CEA showed an inferior sensitivity to the other markers (51% vs 72% and 71%). We concluded that these markers can be useful to monitor the therapy in pts with elevated levels pretreatment. We believe interesting to determine them together pretreatment, because at least 1 of the 3 was elevated in 89% of pts.

1264 POSTER

CYTOKERATIN 19 SOLUBLE FRAGMENTS (CK19) DETERMINATION IN PATIENTS WITH NON-SMALL CELL LUNG CANCER (NSCLC): COMPARISON WITH TPA, CEA, SCC AND NSE

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Preliminary studies have shown a correlation between CK 19 high levels and NSCLC. In order to evaluate the clinical role of this tumour marker, we have compared CK 19 with TPA, CEA, SCC and NSE in a series of 72 patients with newly diagnosed, histologically proven NSCLC (39 squamous cell, 33 adenocarcinoma); all patients underwent surgical resection. CK 19 serum levels were determined by means of the Enzymun Test Cyfra-21.1 (Boehringer Mannheim). ROC curves were defined for each tumour marker; Youden test, Mann-Whitney U test and the Kruskal-Wallis test were used for statistical analysis. Our data show that CK 19 is an accurate tumour marker in patients with NSCLC and it displays a close association with the squamous cell histotype. However, CK 19 does not offer better informations than CEA in adenocarcinoma and TPA in squamous cell carcinoma.

1265 POSTER

THE DIAGNOSTIC POTENTIAL OF "ONCOTEST" AS A METHOD FOR POPULATION SCREENING TO DETECT MALIGNANT TUMORS

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Our method of marker diagnosis of human malignancies is based on detection of Ca^{+2}-Histone complexes in peripheral blood which enter circulation from foci of primary and/or secondary malignant neoplasia as a result of the former split from tumor cell DNA (PCT/UA/00007, 031293, International Bureau of WIPO, Geneva, Switzerland). We performed screening of 3820 employees in Kiev: results of ONCOTEST were correct for 3800 PA (true negative-3773, true positive-17) with 20 errors (false positive-18, false negative-2). Morphologic verification of 17 true-positive results revealed 8 cancers: esophageal-1, gastric-1, rectal-1, breast-1, lung-1, thyroid-1, uterine-3, osteosarcoma-1, Ewing's sarcoma-1, soft tissue sarcoma-2, lymphosarcoma-3 and lymphogranulomatosis-1.

1266 POSTER

USE OF SERUM THYROGLOBULIN FOR MONITORING THE EFFECT OF CHEMOTHERAPY AND IRRADIATION IN DIFFERENTIATED THYROID CANCER

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Standard evaluation of the effect of chemotherapy (CHT) and/or irradiation (RT) by measuring tumor diameters can be misleading due to tumor necrosis. The aim of this work was to study the value of sequential Tg measurements for monitoring the effect of treatment in inoperable differentiated thyroid cancer (DTC).

From 1985–1993, 48 cycles of treatment were applied in 36 patients (27 females, 9 males, age 33–81 years) with primarily inoperable, recurrent or metastatic DTC. Serum Tg measurements were performed before therapy (CHT or CHT and RT), 24, 48, 72, 96 hours and 3 weeks after treatment. The changes in Tg levels, tumor diameters, cytomorphology and DNA distribution pattern after treatment were evaluated.

In 39/48 cycles the results of monitoring the effect of treatment by serum Tg measurements were in agreement with the results of other methods. In 6 patients elevated serum Tg after treatment were observed, which could classically be interpreted as tumor progression. However, the other methods indicated excellent treatment effect. In latter increased Tg was the consequence of tumor necrosis and increased efflux of Tg. Consequently, the actual sensitivity of monitoring treatment by Tg measurements was 93.7% (45/48). Beside the changes in cytomorphology and DNA distribution pattern, the Tg levels can be an early indicator for effectiveness of CHT.

1267 POSTER

EXPRESSION OF HER-2/NEU EGFR, HORMONE RECEPTORS, CATHEPSYN-D AND PLOIDY IN NORMAL AND NEOPLASTIC GI TRACT TISSUES

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Six biochemical parameters, recognized as being prognostic factors in breast cancer, were evaluated on fresh samples of human GI tract tumors to better define the biology and natural history of such neoplasms. Levels of expression of HER-2/neu oncogene and epidermal growth factor receptor (EGFr) protein products, ER, PgR, cathepsin-D and ploidy were determined in 16 gastric and 39 colorectal tumors and compared with normal samples from the same subjects. In 56% of gastric, 61% of colon and 35% of rectum carcinomas HER-2/neu gene product p185 was significantly overexpressed as compared to normal tissues. On the contrary colon and rectum tumors expressed significantly lower levels of EGFr than normal in 60% of cases. Very low levels of ER and PgR were detected in all the samples (normal and malignant) tested. 75% of tumour tissues showed a significant higher cathepsin-D content compared to the respective normal sample while an aneuploid DNA profile was documented in 72% of neoplasms. Overall, change of the markers evaluated seems to be a specific phenomenon of certain GI carcinomas. Higher EGFr levels in normal than malignant tissues suggest that EGFr can be implicated in the process of growth and differentiation of the normal gastrointestinal mucosa. Further studies on a larger number of cases along with an adequate follow-up of patients are needed to define the role of these markers in the pathogenesis of GI tract neoplasms and its prognostic significance when considered together with other major risk factors.

1268 POSTER

IS AN INCREASED CARCINOEMBRYONIC ANTIGEN (CEA) CONCENTRATION IN PERICARDIAL FLUID AN INDICATION OF MALIGNANT PERICARDITIS?

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The aim of the study was to evaluate the role of CEA in pericardial fluid (pf) for the recognition of malignant pericarditis. 30 patients (pts): 15 men, 15 women, median age 61 years with large pf of unknown origin were treated with pericardiocenthesis, cathether instillation and pf drainage. In 21 of them malignant pericarditis was diagnosed. The primary site of tumor was lung in 19 pts, pleura in 1 pt and large bowel in 1 pt. In 9 pts the cause of pericarditis was benign. CEA was measured with radioimmunoassay. Cut off value was calculated at 7 ng/ml. Elevated CEA levels were found in 18/21 malignant pf and 0/9 nonmalignant pf. Mean CEA values were: 52.29 ± 40.66 ng/ml for malignant pf and 2.21 ± 1.28 ng/ml for nonmalignant pf. We conclude that CEA determination in pf is very helpful in recognition of malignant pericarditis.

1269 PUBLICATION

THE VALUE OF FERRITIN IN THE DIFFERENTIAL DIAGNOSIS OF MALIGNANT EFFUSIONS

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The diagnostic value of ferritin in pleural effusion or ascite was studied in 147 patients (89 males and 58 females). One hundred and fifty-one samples (99 pleural effusions and 52 ascites) were examined. The effusions comprised 4 groups: transudate, tuberculous, malignant and benign non-tuberculous exudate. Median ferritin levels in effusions were as follows: 67 ng/ml (27 cases) in transudate, 889 ng/ml (47 cases) in tuberculous, 998 ng/ml (51 cases) in malignant and 805 ng/ml (26 cases)