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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)