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A PHASE II STUDY OF EPIRUBICIN IN COMBINATION THERAPY OF SMALL CELL LUNG CANCER (SCLC)

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47 untreated patients with histologically proven SCLC were included. Patients characteristics were: median age 53(29-68), PS>70, 41 male and 6 female, 40 with limited disease (LD) and 7 with extensive disease (ED), evalubale or measurable disease. The treatment regimen consists of Epirubicin 30mg/m^2 on d1+8, Etoposide 80mg/m^2 on d1 to 5 and Cisplatinum 80 mg/m^2 on d2, repeated every 3 weeks. The patients received 165 cycles chemotherapy totally. The overall response rate was 59.6%, including 19% CR. In LD stage CR is 20% and PR 45%. In ED stage one patient is with CR /primary tumor and gl.suprarenalis/ and 1 with PR.

The toxicities were mild and the most common: nausea, vomiting and alopecia in 100% with only one patient with hematological toxicity: neutropenia grade IV. No cardiotoxicity was observed.

Our conclusion is that this regimen is active in SCLC with acceptable toxicity. The impact on survival remains to be determined.

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COMPARISON OF CYTOKERATIN FRAGMENT 19 (CYFRA 21-1), TISSUE POLYPEPTIDE ANTIGEN (TPA) AND CARCINOEMBRYONIC ANTIGEN (CEA) AS TUMOR MARKERS IN LUNG CANCER

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To evaluate the diagnostic value of the serum cytokeratin 19 fragment (CYFRA 21-1) and compare it with carcinoembryonic antigen (CEA) and tissue polypeptide antigen (TPA) in lung cancer, we investigated the sera of 161 patients (58 with benign pulmonary disease and 103 with lung cancer) using immunoradiometric assay. Sensitivities for CYFRA 21-1, CEA and TPA (using 3.5 ng/ml, 5.0 ng/ml, 110 U/l, respectively, cut-off values) in lung cancer were 64%, 47%, and 61%, respectively. Positive CYFRA 21-1 levels were identified in 75% of patients with squamous cell carcinoma (n = 36), in 67% with adenocarcinoma (n = 45), in 17% with large cell carcinoma (n = 6), and in 50% with small cell lung cancer (SCLC) (n = 16). However, CYFRA 21-1 levels were not significantly different between squamous cell carcinoma and the other histological types. Sensitivity of the CYFRA 21-1 and/or CEA combination (77%), CEA and/or TPA combination (77%), and CYFRA 21-1 and/or CEA and/or TPA combination (82%) were significantly higher than that of single CYFRA 21-1 masurement. Elevated CYFRA 21-1 levels were observed in 44% of stage I and II (n = 18) and 72% of stage III and IV (n = 69) patients with non-small cell lung cancer (p< 0.05). The positive rate of CYFRA 21-1 in tumor stage I and II was only 44% (CEA: 22%, TPA: 44%), i.e. the markers under study cannot be used for the diagnosis of early stage disease. A significant inter-marker correlation was observed between CYFRA 21-1 and TPA (n = 103, r = 0.448, p < 0.0001), but not between CYFRA 21-1 and CEA (n = 103, r = 0.025, p = 0.8), nor between CEA and TPA (n = 103, r = 0.082, p = 0.41). Our results indicate that CYFRA 21-1 may be a useful tumor marker in lung cancer. The CYFRA 21-1 and/or CEA combination could be recommended as the best combination for increasing the diagnostic sensitivity. In addition, CYFRA 21-1 may contribute to the monitoring of lung cancer.

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LOCALIZED MALIGNANT MESOTHELIOMA IN HUNGARY

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The localized malignant mesothelioma (LMM) cases were selected from the data recording of pulmonary cases. From 1982 to 1994 there were 9 histologically proved LMM cases in Hungary. Five of them were asymptomatic, and the tumors were removed surgically in all the 9 cases. Invasion to the lung, to the chest wall or both was found in 3, 2 and 1 cases respectively. The histological subtype of LMM cases were sarcomatousus and epithelial in 2-2, and mixed in 5 cases. Follow up was obtained in 8 patients: 5 of them were cured, 2 patients died of local recurrences and 1 of distant metastases.

Summarized: The incidence of LMM is less than 1 o/oooooo in Hungary. The disease was radically cured with surgery in more than half of the cases. There was no significant relation with the mode of detection, nor the expansion and the histological features of the tumor and the survival time.

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FLUORESCENCE BRONCHOSCOPY IN EARLY DETECTION OF LUNG CANCER.

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Laser-induced fluorescence from normal and neoplastic tissue differs in shape and intensity and can be used for diagnostic purposes. In this view a new device, LIFE imaging system (Xillix Co., Vancouver), is available for clinical application in the tracheo-bronchial tree ad it has been used-in 140 patients at high risk of lung cancer at INT of Milan (Italy). After a white light bronchoscopy, the patients were submitted to fluorescence bronchoscopy and the findings of both examinations have been classified in 3 cathegories: class I or normal, class II for alterations suggesting inflammation or metaplasia and class III for neoplastic mucosa. All II and III sites have been biopsied for histologic examination: a comparison between histologic results and white light or fluorescence bronchoscopy has been performed for assessing sensitivity and specificity of the two exams. Squamous intraepithelial neoplasia has been detected in 19 patients with a sensitivity of 74% for white light bronchoscopy and 100% for fluorescence bronchoscopy. Specificity of white light and fluorescence bronchoscopy was 92% and 79%, respectively. These data suggest that fluorescence bronchoscopy improves accuracy of endoscopic examination in detecting early lung cancer.

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CHEMOTHERAPY INDUCED LEUKOPENIA AS A PREDICTOR OF RESPONSE IN SMALL CELL LUNG CANCER (SCLC)

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The correlation between chemotherapy (CT) induced toxicity and therapeutic efficacy in cancer patients (pts) has been studied only occasionally. Our aim was to evaluate the possible relationship between CT induced leukopenia and response to treatment in 238 SCLC pts treated within two prospective multicenter studies. CT regimens included CEE (cyclophosphamide, etoposide, epirubicin; in 128 pts) or VEC (vincristine, epirubicin, cyclophosphamide; in 110 pts), both given every 3 weeks. The highest score of leukopenia within the first 2 CT cycles was recorded. The response was evaluated after a median of 4 cycles (range 2-5). The objective response rate (CR and PR) for the whole group was 68%. Response was seen in 92% of pts who developed leukopenia and in 43% of pts whose WBC remained normal (p<0.000). In multifactorial analysis including also other treatment- and patient-related factors, independent correlation with response to CT was found for leukopenia (p<0.000, coef=0.2), the CT regimen used (p=0.002, CEE being more toxic and more effective) and the number of CT cycles. Response was not related to patient sex, age, performance status, pre-study weight loss, extent of disease and dose intensity. No significantly better survival was observed in pts who developed leukopenia during the first 2 cycles (p=0.09). Additional analysis showed however, that both response rate (p<0.000) and survival (p=0.009) was better in pts who developed leukopenia during the first 4 CT cycles. It seems that there is a close relationship between CT induced leukopenia and tumor response. Further studies concerning other tumors or other side effects are warranted.

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THE ROLE OF HISTAMINE H1-RECEPTORS IN THE NEUROMODULATION IN HUMAN LUNG ADENOCARCINOMA

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An abnormality in autonomic neural control in lung cancer has not yet been investigated. In the present work histamine H1- and H2-receptors have been examined in human lung parenchyma obtained at the resection of tuberculoma patients within the normal tissues limits and the resection of adenocarcinoma patients. The Scatchard analysis indicated the activation of histamine H1-receptors which may lead to the reduction of beta-adrenoceptors and the enhancement of muscarinic cholinergic receptors in cancer lung parenchyma, that has been demonstrated in our previous work. The above findings suggest the possibility of the interaction between neural and inflammatory systems in human lung adenocarcinoma and may shed light on the pathogenesis and treatment of lung cancer.