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SMALL CELL LUNG CANCER AND CNS-METASTASES - RESULTS OF COMBINATION CHEMOTHERAPY WITH CARBOPLATIN/ETOPOSIDE/VINCRISTINE (CEV)

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Introduction:
CNS is one of the main locations of metastases in disseminated SCLC. In our hopitel out of 600 pts. in the past 5 years 8,5 % had CNS-metastases. Prognosis seems worse in comparison to pts. with extensive stage disease, but without CNS-involvement. To look for the efficacy of chemotherapy with CEV in pts. with primary CNS-metastases we performed a phase-II-trial.

Patients and methods:
51 pts. with SCLC + CNS-metastases received a combination chemotherapy with CEV (Carboplatin/Etoposide/Vincristine).
Male/female: 34/15. Perf.-status (Karnofsky): >80/<80: 33/16.

Response: CR + CR/PR:18,4 % + 57,9 %

MST:
All patients 6 months, responder 10 months and non-responder 2 months. The most important prognostic factors are performance-status and the number of locations of metastases.

Conclusion:
Patients with SCLC anc CNS-metastases have a comparable prognosis according to remission-rate and survival to pts. with disseminated SCLC without CNS-metastases. Perf.-status is the main predictive parameter for response and survival. Combination chemotherapy is the therapy of choice also in pts. with SCLC and CNS-metastases, probably combined with cranial irradiation.

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PERICARDIAL METASTASES IN SMALL CELL LUNG CANCER-PATIENTS NEW APPROACHES TO THE DIAGNOSIS AND TREATMENT.

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Two- dimensional echocardiography is a very useful method for the detection of pericardial metastases. 64 PTS with SCLC were studied by echocardiography before chemotherapy. Pericardial abnormalities were found in 19 PTS /30%/ As well as metastases in other organs they have diseappeared in 10 PTS during chemotherapy. During the follow-up pericardial metastases were observed for the first time in 11 PTS /17%/ with normal previous echocardiographic examination. The autopsy confirmed the ECHO-findings in 7 cases The neoplastic involvement of the pericardium was also found in 32% of cases of the 50 autopsies of another group of SCLC-PTS. Our data show that pericardial metastases in SCLC are frequent /30%/. They disappeared during chemotherapy as well as metastases in other organs. The pericardial metastases can be the sole site of the cancer involvement.

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TNM STAGING OF SMALL CELL LUNG CANCER

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Small cell lung cancer has generally been classified as either limited or extended disease. Recently it has been recommended to use the new TNM-classification (UICC 1987), when the treatment involves local modalities. In the present study, we have investigated whether it is possible to stage small cell lung cancer according to the TNM-classification by use of radiologic examinations, bronchoscopy and mediastinoscopy. Twenty patients were randomly selected ouf of 199 patients with limited stage small cell lung cancer treated in a randomized prospective trial. None of the patients had metastases. Chart informations on broncho-mediastinoscopy as well as x-ray pictures were examined by an independent observer. It was not possible to evaluate tumour invasion into pleura, diaphragm, mediastinal pleura, mediastinum, parietal pericardium, heart, great vessels, oesophagus and vertebral body in any of these patients. T-stage classification was possible in 84% of the patients, however, only if these problems were not taken into account. The T-stage is therefore likely underestimated in some patients classified as T1/T2. By use of mediastinoscopy, 75% was classified as N0, and 25% as N2 + N3. By use of radiologic examination, 10% was classified as N0, 45% as N1, 25% as N2 + N3, and 20% as Nx. Agreement between the results of x-ray and mediastinoscopy was only obtained in 30% of the patients. TN-staging of patients with small cell lung cancer according to TNM-classification is not possible based on radiologic examinations and bronco-mediastinoscopy and other investigations such as CT or MR imaging are needed.

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MODERATE DOSE INTENSIFICATION OF CARBOPLATIN AND ETOPOSIDE AS FIRST LINE COMBINATION CHEMOTHERAPY IN SMALL CELL LUNG CANCER

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To test the feasibility of moderate dose intensification of Carboplatin and Etoposide as first line combination chemotherapy in small cell lung cancer (SCLC), without the aid of haemopoetic growth factor support, a pilot study was initiated in which 54 previously untreated patients received the following regimen : Carboplatin 600 mg/m^2 IV on day 1 and Etoposide 120 mg/m^2 IV days 1-3 for two 28 day cycles, followed by an elective dose reduction of Carboplatin to 400 mg/m^2 and Etoposide 100 mg/m^2 for a further 2 cycles. Limited disease (LD) patients achieving a complete remission (CR) or partial remission (PR) subsequently received thoracic radiotherapy and were then randomised to receive prophylactic cranial radiation (PCI) or no further treatment. Fifty-one patients were assessible for response and toxicity, with 3 non-treatment related deaths prior to completion of the first cycle. Forty-six patients (90%) obtained an objective response including 93% (50% CR) of LD patients and 89% (5% CR) of ED patients. Median response duration was 9 months for LD and 6 months for ED. Median survival for LD patients was 14.5 months and 9 months for ED patients. The major toxicity was haematologic with WHO grade 3-4 leucopenia and thrombocytopenia occurring in 69% and 65% of patients respectively. Twelve patients (23%) had a dose reduction at some stage during treatment due to neutropenic infection or severe thrombocytopenia. Three patients developed severe life threatening infection but there were no toxic neutropenic deaths. Non-haematologic toxicity was minimal and in particular there was no significant renal or neurotoxicity. Overall the treatment was well tolerated and this study confirms that moderate dose intensification of these agents can be successfully achieved with standard supportive care without the need for haemopoetic growth factor support. This regimen is highly active in terms of response rate, however overall response duration and median survival figures appeared no better than with conventional chemotherapy.

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ADJUVANT THERAPY FOR NON METASTATIC LUNG CANCER PATIENTS : A METHODOLOGICAL LITERATURE REVIEW.

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We have reviewed the English and French literatures about adjuvant therapy for non metastatic lung cancer patients. We identified 32 randomized trials testing this concept for non small cell lung cancer (NSCLC) and 14 for small cell lung cancer (SCLC). In NSCLC, 13 of these studies compared surgery versus surgery + immunotherapy, 6 surgery versus surgery + chemotherapy, 4 surgery versus surgery + radiotherapy and 9 radiotherapy versus radiotherapy + chemotherapy; in SCLC, 12 studies tested the value of irradiation combined to chemotherapy and 2 the value of immunotherapy combined to the association chemotherapy-radiotherapy. Our main findings about the methodology, the design and the reporting of these trials are the following : no study but three justifies its sample size by giving statistical considerations but otherwise statistical methods for analysis are generally well described as well as the randomization procedures. In NSCLC, only about 30% of the studies have a sample size large enough to demonstrate a relative increase of 50% of long term survival rate in the experimental arm compared to the control arm. In SCLC less than 25% of the studies were able to show a relative increase of 100% of the same rate. Methods for disease extent evaluation and patients follow up were rarely well described. Despite the often small power of the studies, crude numbers of deaths allowing the calculation of a combined odds ratio are given in only 47% of cases in NSCLC and in 40% in SCLC. Furthermore, the trials are quite different in design, methodology, treatment (doses, specially dose intensity of chemotherapy in SCLC, timing) to lead to any valid conclusion when aggregated.

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A RANDOMIZED TRIAL COMPARING IN SMALL CELL LUNG CANCER (SCLC) INDUCTION CHEMOTHERAPY BY IFOSFAMIDE AND ETOPOSIDE WITH ADRIAMYCIN (IVA) OR EPIRUBICINE (IVE) : AN EUROPEAN LUNG CANCER WORKING PARTY REPORT.

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New active cytostatic agents - analogs of active known drugs - have been identified during the last decade against SCLC but prospective trials comparing analogs are rare. Our group compared adriamycin (45 mg/m^2 d1 iv) to epirubicin at an equivalent dosage (60 mg/m^2 d1 iv) in combination with ifosfamide (1.5 g/m^2 d1-3 iv) and etoposide (80 mg/m^2 d1-3). Six courses were given at 3 to 4 weeks intervals. Then responders were randomized for maintenance chemotherapy. The purpose of the present report is to compare the 2 induction regimens in terms of antitumoral response and toxicity. 111 patients were registered between July 90 and September 91 :

	IVA	IVE
patients registered/evaluable	56/49	55/49
Disease : limited/extensive	23/26	24/25
Best responses : complete + partial	5 + 34	3 + 36
Main toxicities (grades III-IV)		
leucopenia/thrombopenia	64 %/9 %	69 %/4 %
Toxic deaths	4 (8 %)	0

All toxic deaths were due to infections complicating neutropenia.
In conclusion, IVE appeared as active but less toxic than IVA.