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MONOCLONAL ANTIBODIES (MoAbs) DIRECTED AGAINST THE NEURAL CELL ADHESION MOLECULE (NCAM) IMPROVE THE DETECTION OF SMALL CELL LUNG CANCER (SCLC) METASTASIS IN BONE MARROW ASPIRATES (BMA) COMPARED WITH CONVENTIONAL HISTOLOGY.

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Eighty-seven BMA were collected from 40 pts with SCLC. BMA were collected bilaterally from posterior iliac spines in 39 pts and unilaterally in one. From 37 of these 40 pts, 58 bone marrow biopsies were also obtained (18 bilaterally). Briefly, 3-5 mls of marrow were aspirated in heparinised syringes, diluted with RPMI, layered over Ficoll-Paque, the cell layer collected and the cell pellet cytospinned. A standard ICH method (APAAP) was used with 2 MoAbs, NCC-LU-243 (IgG2a) and NCC-LU-246 (IgG1) belonging to cluster 1, which recognizes NCAM. Adequate control study were always performed. In BMA reactive cells were detected in 37/87 specimens (42.5%), while only 7/58 bone marrow biopsies (12%) showed metastatic involvement (p=0.0001). Also in Limited Disease (LD) the use of MoAbs in our series was an improvement on conventional histology, because 7 out of 16 pts (44%) clinically and histologically staged as LD, had positive BMA (p=0.006). Among the 19 pts with positive MA, 17 had biopsies taken, 4 positive and 13 negative. Among the 25 pts with negative BMA, 23 had also negative biopsies and just 1 positive. Only in 1 case was the result different between the 2 sites of aspiration. A negligible difference was found between the 2 MoAbs. In conclusion: in our series the use of MoAbs significantly increased the detection of bone marrow involvement compared with conventional histology, suggesting that a large proportion of pts are otherwise understaged.

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A PHASE II TRIAL OF CARBOPLATIN (C), IFOSFAMIDE (I),ETOPOSIDE (E) AND VINCRISTINE (V) IN SMALL CELL LUNG CANCER.

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From January 1989 through June 1991, 44 untreated patients (pts) with SCLC have entered a trial to evaluate the CIEV scheme. Pts were treated with Carboplatin 300 mg/m2 IV d1, Ifosfamide 5 gr/m2 d1 with Mesna, Etoposide 120 mg/m2IV d1-3 and Vincristine 0.5 mg/m2 IV d14. Limited Disease (LD) patients also received chest irradiation. Of 44 patients, 41 were male and 3 were female; 27 had LD and 17 had Extensive Disease (ED). 23 were ECOG 0-1 and 21 were ECOG 2-3. The median age was 60.5 (range 42-76). Forty pts are now evaluable for response: 12 pts/40 achieved CR (30%) and 20 pts/40 achieved PR (50%); overall response rate was 80%

	Total(%)	EL(%)	EE(%)	QR(%)	MS(%)
CR	12 (30)	8 (32)	4 (26.6)	7.5	12
PR	20 (50)	13 (52)	7 (46.6)	3.5	8
Total	32 (80)	21 (84)	11 (73.3)	5.5	10

The median response duration was 5 mo (7.5 mo LD and 3.5 ED). There were 12 CR relapsed (33% local, 58% distance and 8% both); the LD distribution was 4/8 local, 3/8 distance and 1/8 both and for ED patients 4/4 distance. The median survival time was 10 mo (12 mo LD and 8 mo ED). The major toxicity was hematologic (by WHO) with leukopenia grade 3-4 ocurring in 4.8%, thrombocytopenia grade 3-4 in 2.4% and anemia grade 3-4 in 3.2%. Nausea and vomiting were mild. Two pts presented hemorrhagic cystitis and 1 pts mild neurologic toxicity. No hepatic or CNS disturbance or renal failure was noted. 4 pts died early.

CONCLUSIONS: 1) The CIEV scheme is well tolerated in a outpatient setting. 2) Response rate are in the range previosly reported but the CR rate is low. 3) These results suggest that future protocols will require evaluation with higher dose of Carboplatin and Etoposide trying to improve the CR rate and MS.

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TUMOR MARKERS IN FOLLOW UP OF THERAPY IN SMALL CELL LUNG CANCER (SCLC)

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We followed the surgical,hemotherapeutic,irridation or combined therapy in 32 patients (pts.) with verified SCLC by tumor markers values.We compared those values in previously untreated pts. and in pts. with clinical stabilized disease after therapy.CEA,CA19-9 and NSE were determined by IRMA CIS and counted by computer processing.Tumor markers values and high values (%) were:

	NSE (ug/l)	CEA (ng/ml)	CA 19-9 (U/ml)
cut off value(50):	10,3	8,2	33,6
-untreated SCLC(32)	22,1±16,5	19,7±25.3	48,4±31.3
	75%(24)	56,2%(18)	62,5%(20)
-treated SCLC(26)	13,65±13,1*	5,7±8,7*	22,5±9,6*
	42,3%(11)	11,5%(3)	19,2%(5)

* p/ 0,005. The simultaneous determination of CEA,CA19-9 & NSE in untreated group gave sensitivity of 90,6%(29), and in treated group 61,5% (16). We recomand the simultaneous determination of tumor markers in SCLC as a valuable parametar of clinical staging in desease and more sensitive for monitoring the clinical stabilized disease under therapy.

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ANALYSES OF LONG TERM SURVIVAL IN SMALL CELL LUNG CANCER (SCLC)

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From 1981 to 1988 a total of 1179 patients (pts) with SCLC were included in four consecutive multicenter German trials. After minimum follow up of 3 years, an analysis of long term survival has been performed. The main characteristics of the pts. achieving a 3 year survival are shwon on the following Table.

		No pts.	No 3y sur.	% 3y sur.
Stage	non-met.	663	61	9,2
	met.	516	9	1,7
Sex	female	28	180	15,5
	male	42	999	4,2
Performance	50-70%	241	7	2,9
(Karnofsky)	80-100%	938	63	6,7
LDH	<240	635	46	7,2
	>240	467	16	3,4
NSE	<12.5	291	28	9,6
	>12.5	340	17	5,0

During the further follow up, 24 of the 70 3 year survivors died. Main causes were recurrent SCLC in 15 pts., second malignancies in 4 pts. and non-cancer related reasons in 6 cases. Fourty-six pts are still alive, 44 with stable CR and 2 with relapse of disease. Only 2 pts. with metastatic disease achieved stable CR, one with bone metastases and one with a spleen lesion. Thus, among the known prognostic factors in SCLC only extent of disease precisely predicts long term disease free survival and therefore may be usefull as a selection criteria for different treatment protocols.

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STANDARD (SC) VS. PALLIATION CHEMOTHERAPY (PC) IN METASTATIC SMALL CELL LUNG CANCER (MSCLC)

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Patients with MSCLC have nearly no chance of cure. Therefore, in a multicenter German trial e less toxic PC was compared to SC with regard to survival and quality of life. SC consisted of AIO (adriamycine 50 mg/m2 d1, ifosfamide 1500 mg/m2 d1-5, vincristine 2 mg d1) alternating with CE (carboplatin 300 mg/m2 d1, etoposide 120 mg/m2 d1-3) and PC consisted of EV (etoposide 150 mg/m2 d1-3, vincristine 2mg d1). Both regimens were given for 4 cycles in 4 week intervals. Until now, 186 pts have been included and interim analyses was performed after 150 pts (50% of the projected sample size) had died. CR+PR after 4 cycles was 48% for SC and 24% for PC. However, during induction therapy 50% of the pts with PC were crossed over to standard polychemotherapy due to nonresponding disease. This may be the reason why median survival did not differ between both groups (6.5 mo). Toxicities like nausea/vomiting, myelosuppression and infections were higher in SC. Before each cycle pts were requested to fill in a questionaire of quality of life. Improvements in physical functioning, disease related symptoms, and fatique/malaise were more pronounced in SC than in PC. In conclusion, this preliminary analysis indicates that pts with SC had a better tumor response and improvement of quality of life than pts with PC, but survival did not differ between both groups.

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TREATMENT OF REFRACTORY OR RECURRENT SMALL CELL LUNG CANCER (SCLC) WITH CYCLOPHOSPHAMIDE, CISPLATIN AND VINCRISTINE (A NON-CROSS-RESISTANT REGIMEN).

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Most patients with SCLC relapse. Treatment of refractory or relapsing disease has been considered unsuccessful: response rates have been low and survival unaffected by treatment.20 recurrent and fully evaluable SCLC patients are analysed. All patients were males. Median age was 59 years (range 34-75). Previous chemotherapy included VP-16, doxorubicin and methotrexate (VDM) in all patients. Four patients with limited SCLC had recieved thoracic radiotherapy. Concurrently with it, doxorubicin and methotrexate had been substituted by cyclophosphamide and vincristine. All patients had PS (WHO) equal or less than 2. Seven patients were refractory to VDM (had failed to attain a PR).Treatment regimen consisted of : cyclophosphamide 750 mg/m2, cisplatin 75 mg/m2, vincristine 2 mg IV day 1. Courses were repeated every 3 weeks on an outpatient basis for a maximum of six.There were 6 RP and 1 RC (35% response rate). 4 of these pts were refractory to first line therapy. The median duration of remission was 21 weeks (range 9-112+). Median survival time of responders was 31 weeks (range 31-112+). The median survival time for all patients was 18 weeks (range 8-112+).One patient is in continuous complete remission for more than 2 years. Toxicity was mild. Seven pts (35%) had emesis grade 3. There was only one episode of neutropenic fever. There was no toxic death. This regimen is effective and its toxicity acceptable in recurrent SCLC. It can be studied as first line therapy.