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**ANTI-CEA IMMUNOSCINTIGRAPHY (IS) MIGHT BE MORE USEFUL THAN COMPUTED TOMOGRAPHY (CT) IN THE PRE-OPERATIVE THORACIC EVALUATION OF LUNG CANCER (LC): A comparison between planar IS, single photon-emission CT (SPECT), and radiographic CT.** **GF. Bucchari, A. Biggi, D. Ferrigno, A. Leone, M. Taviani, M. Quaranta. A. Carle Hospital of Chest Diseases, and S. Croce General Hospital, Cuneo, Italy.**

**According to an our recent report (Cancer 1992; 70:749), the IS with anti-carcinoembrionic antigen (anti-CEA) monoclonal antibodies (MA) might have a remarkable staging potential. To compare the diagnostic accuracy of this technique with a more conventional one, we photoscanned 45 LC patients (pts) with Indium-111 (111In)-labeled- F(ab')2 fragments of the murine anti-CEA MA FO23C5. Pts were pathologically assessed for loco-regional invasion of lung cancer. Both plan and SPECT images were obtained. Additionally, CT of the thorax (contiguous computerized axial tomographic slices, 10 mm thick, from the lung apices to the upper abdomen), and other routine tests of pre-operative evaluation were obtained. On the basis of 37 (N1,T3,and T4), 38 (N2), and 12 (N3) pathologically documented sites, an accuracy of 65,76,92,78, 89% (planar IS images); 68,78,92,78, 86% (SPECT IS images); and 62,68,42,78, 84% (CT images) was calculated (figures are relevant to N1,N2,N3,T3, and T4 disease, respectively). If current findings will be confirmed in future studies, anti-CEA IS might become a valid alternative to CT.**

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CONCOMITANT CISPLATIN, ETOPOSIDE AND RADIOTHERAPY FOR LOCALLY ADVANCED NON-SMALL CELL LUNG CANCER (NSCLC). F. Reboul, P. Vincent, B. Chauvet, Y. Brewer, C. Félix Faure, M. Taulelle. Lung Cancer Treatment Unit. Clinique Sainte Catherine. BP 846. Avignon 84082 France.

Since July 1989, we have treated 130 patients with locally advanced or medically inoperable NSCLC by concomitant chemoradiotherapy. In our first study, 85 patients received 40 grays to the mediastinum followed by a tumor boost of 30 grays with concomitant cisplatin at a dose of 20 mg/sqm/24 hr over 5 days during the 2nd and 6th radiation weeks. Complete response rate was 66%. With a median follow-up of 27 mos, actuarial survival at 1, 2 and 3 yrs was respectively 48.2%, 27.5% and 25%. Disease-free survival was 26% at 2 and 3 yrs. These results compare favorably with standard radiation therapy alone and are very similar to other concomitant cisplatin-radiotherapy trials. However, they remain unsatisfactory since concomitant cisplatin is likely to act through better local control but has little impact on subclinical disease. Therefore, we initiated in Feb. 1992 a second study in which etoposide at 50 mg/sqm/d for 5 days was added to cisplatin for 4 cycles. The first 2 cycles of chemotherapy were delivered during the 1st and 5th weeks of radiotherapy, followed by two additional cycles at weeks 8 and 11. 45 patients have now been enrolled in this study and 24 patients have sufficient follow-up for a first analysis. Overall response rate is 87.5% with 62.5% complete response. With a median follow-up of 9.7 mos (6.6-11.7), overall survival is 87% at 6 mos and 74.5% at 9 mos with a corresponding disease-free survival of 78.3% at 9 mos. Toxicity was acceptable. Although preliminary, these results appear to be improved over our first study which could be related to a significant reduction in early distant metastasis while sustaining a high level of local control.

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CISPLATIN (CDDP)-ETOPOSIDE VS CDDP-MITOMYCIN-VINDESINE VS CDDP-MITOMYCIN-IPHOSPHAMIDE IN ADVANCED NON SMALL CELL LUNG CANCER (NSCLC). A PROSPECTIVE RANDOMIZED TRIAL OF THE ITALIAN ONCOLOGY GROUP FOR CLINICAL RESEARCH.(GOIRC)

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To evaluate the efficacy of a 3 drug regimen vs a 2 drug CDDP based combination in treatment of NSCLC we conducted a 3 arm randomized parallel trial comparing CDDP (120 mg/sqm d 1) Etoposide (100 mg/sqm dd 1-2-3) every 3 wks (PE-arm A) to CDDP (120 mg/sqm every 4 wks) + Mitomycin (8 mg/sqm dd 1-29-71) + Vindesine (3 mg/sqm dd 1-8-15-22 then every two wks) (MVP-arm B) and to CDDP (120 mg/sqm d 1) + Mitomycin (6 mg/sqm d 1 ) + Iphosphamide (3 gr/sqm d 2) every 3 wks (MIP-arm C). From May 1989 to April 1992, 394 consecutive previously untreated patients (pts) with NSCLC stage IIIB and IV entered the trial; 372 are evaluable for survival and 351 for response.

| Results: | PE(A) 111 pts, | MVP (B) 120 pts, | MIP (C) 120 pts |
|---|---|---|---|
| Overall Response %: | 24% (0 RC) | 37.5% (5 RC, 4%) | 40% (4 RC, 3.3%) |
| Median Surv. Oct. 92: | 29.8 wks | 43.4 wks | 36.2 wks |

The response rate was significantly better for both the 3 drug regimens compared with PE; B-A: 0.132 (C.I. 95%: 0.016 - 0.2489; C-A: 0.157 (C.I. 95%: 0.039 - 0.275) Logistic regression model showed a significantly better response in pts with a good P.S. and in Stage IIIB; a significant interaction between treatment and stage was found: pts with stage IV obtained a better response if treated with either of the 3 drug combinations. Main toxicity consisted of myelo-suppression: neutropenia grade III-IV was recorded in 23% (arm A); 29% (arm B) and 36% (arm C) (p.=n.s.). Thrombocytopenia grade III-IV was worse in arm C: 21% vs 13% (arm A) and 7% (arm B) (p. < 0.008). Nephrotoxicity grade III-IV was more common in arm C: 9%. Toxic deaths were 11 (3%): 3 in arm A, 5 in arm B, 3 in arm C. Survival estimates are unconclusive at this time of follow-up. From our data, the 3 drug containing regimens MVP-MIP, appear significantly better than 2 drug combination PE in treatment of advanced NSCLC.

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EFFECTIVE CISPLATIN-VINCA ALKALOID COMBINATIONS AS NEOADJUVANT CHEMOTHERAPY FOR STAGE III NON SMALL CELL LUNG CANCER (NSCLC).

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From 4/87 to 7/92, 116 consecutive previously untreated stage III NSCLC patients (pts) received 2 to 4 courses of 4 different Cisplatin/Vinca (Vindesine or Vinorelbine) based combinations (ATTIT 1-2-3-5, ASCO 89, 90, 91, 92). Pts characteristics: median age 57 (38-75); 106 males (91%); performance status (KI): 60-70% 21 pts, >70% 95 pts; histology: squamous 66 pts (57%), adeno 25 pts (22%), large cell 21 pts (18%), adenosquamous 4 pts (3%); AJCC TNM stages: IIIa 60 pts (52%) (N2: 46 pts), IIIb 56 pts (48%). Activity: 52/116 pts achieved OR (45%; 7 CR, 45 PR), 53% in stage IIIa and 36% in stage IIIb (p=0.06); 49/52 pts with OR had an initial KI >70%. Further treatment: 26 pts (22%) all CT responders, 19 IIIa pts (31%) and 7 IIIb pts (12%) (p<0.01), had radical surgery; 7 (6%) were pCR; post-surgical complications were broncho-pleural fistula for 6 pts (fatal in 4 cases). After surgery, the N+ pts received additional RT (12 pts) or CT (3 pts). All 26 non resectable CT responders (14 IIIa pts, 12 IIIb pts) received RT. Median duration of response was 15 months (2-58+) with no difference between resected and irradiated CT responders. Response rate at the end of local treatment was 60%. Survival: with a median follow-up of 33 months (3-66) the overall median survival is 16 months; 18 months for KI >70%, 8 months for KI 60-70% (p<0.001); 23 months for CT responders, 11 months for non responders (p<0.0003). Actuarial survival at 30 months is 30% for resected pts, 36% for irradiated pts, and 12% for non responders pts. Survival was not influenced by stage (IIIa or b), histology or CT protocol. To date, 31 CT responders have relapsed (13 locoregional; 15 metastatic, 3 both). Brain was the main site of metastatic relapse (9/18 pts). Conclusions: 1) 45% OR rate for pts with Cisplatin-Vinca alkaloid combinations confirms single-institution experiences 2) in our study, there is no difference in 30 months survival between resected and irradiated CT responders. Controlled trial comparing for CT responders surgery + RT and RT alone is needed.

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LONG TERM SURVIVAL AFTER CHEMOTHERAPY IN PATIENTS WITH ADVANCED UNRESECTABLE NON SMALL CELL LUNG CANCER (NSCLC) : A REPORT BY THE EUROPEAN LUNG CANCER WORKING PARTY.

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Prognosis of patients with unresectable NSCLC is poor and the palliative effect of chemotherapy remains controversial. Since 1978, the European Lung Cancer Working Party has conducted several trials evaluating various chemotherapy regimens using cisplatin as the central agent. By September 1991, 1052 patients have been included into these trials : 927 (88 %) were evaluable for the present analysis, among which 65 (7 %) were long term survivors (LTS), defined as patients surviving for at least 2 years after the start of chemotherapy. The overall survival of these LTS is at present the following :

| Survival (years) | 2-3 | 3-4 | 4-5 | 5-6 | 6-7 | 7-9 | total |
|---|---|---|---|---|---|---|---|
| alive : | 4 | 2 | 6 | 1 | 2 | 1 | 16 |
| dead : | 40 | 5 | 1 | 1 | 1 | 1 | 49 |
| Total : | 44 | 7 | 7 | 2 | 3 | 2 | 65 |

Prognostic factors analysis was performed by uni-and multivariate methods, considering age, sex, loss of body weight, histological type, prior therapy, Karnofsky PS, disease extent, type of lesion, metastatic sites, and various biological parameters. Limited disease, normal leucocytosis, normal granulocytosis and absence of liver metastases were found to be significant factors associated with better long-term survival at univariate analysis. The impact on long-term survival of response to chemotherapy was evaluated in the 721 patients who survived at least 12 weeks. Objective response (OR) rates were respectively 58 % in survivors ≥ 2 years and 32 % in those surviving < 2 years. In a logistic regression model, OR appeared to be the most significant parameter.

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VINORELBINE (NVB) VERSUS VINORELBINE PLUS CISPLATIN (NVB-DDP) IN ADVANCED NON-SMALL CELL LUNG CANCER (NSCLC) : RESULTS FROM A RANDOMIZED CLINICAL TRIAL (240 PATIENTS)

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Vinorelbine (Navelbine R) is a new 5' nor vinca alkaloid, showing a 29% response rate (RR) with a 33 weaks median survival time (MST) in a phase II study in NSCLC (ASCO, 1988. A.778). Vinca alkaloid plus Cisplatin (DDP) combinations are usually more effective than Vinca alkaloid alone in term of response. Thus, we undertook a randomnized clinical trial, comparing NVB alone (30 mg/m$^2$ weekly) to NVB-DDP regimen consisted of NVB (30mg/m$^2$ weekly) and DDP (80mg/m$^2$ on day 1 repeated q21D).

From October 1989 to July 199, forteen institutions enrolled 240 patients with advanced NSCLC. Randomnization was stratified by institution and stage. Eligibility criteria included : stage III A and B (45%), stage IV (55%) and no prior treatment. no brain metastasis, ps = 0.1 or 2 (21%. 51%. 28%) evaluable or mesurable lesions. 53% of pts had squamous cell carcinoma. 31% adenocarcinoma and 16% large cell carcinoma. The two groups were well-balanced for prognostic factors.

There were 9 inelegible pts. 208 were evaluable for response. the RR was 48% with NVB-DDP and 16% with NVB (p < .001). Median time to progression (TTP) was 20 weeks for NVB-DDP and 10 weeks for NVB. (p = .0001. 2-sided Log Rank Test). The MST was 33 weeks with NVB-DDP and 32 with NVB (p = .48. 2-sided Log Rank Test). The NVB dose intensity was 22.6 mg/m$^2$/w in NVB alone group and 19mg/m$^2$/w in the NVB-DDP regimen.

Nausea and vomitting (G 3-4) were observed in 23% of pts in the NVB-DDP group (5% in NVB group), neurotoxicity (G 2-3) in 18% in NVB-DDP (7% in NVB group). At six months, 89% of NVB-DDP pts experienced grade 4 neutropenia versus 64% in NVB group. Among pts who achieved O.R., 16 refused to continue chemotherapy in NVB-DDP group vs 3 in NVB group.

In conclusion, this phase III study showed a significantly better RR and TTP with the NVB-DDP combination, but survival (MST) was similar in both groups. NVB-DDP was more toxic than NVB alone. Vinorelbine (Navelbine) appears an effective drug in NSCLC, even given as a single agent.