Results: Preoperative concurrent radiochemotherapy showed a partial response in 18 (78%) patients and no change in 5. The main adverse reaction was leukopenia of grade 3 or 4 which was observed in 30%. No severe pulmonary toxicity or esophagitis was observed. An operation was performed in 21 (91%) of the 23 patients consisting of an extrapleural pneumonectomy in 6 patients, a resection of the superior vena cava or vertebral body in 4 each, a carinal resection in 2, and other surgical modalities. Nineteen patients underwent a complete resection. The median survival time of all patients was 27 months and the 1- and 3-year survival rates were 88% and 43%, respectively. There was no mortality related to either the preoperative treatment or operation.

Conclusions: The oral administration of UFT plus cisplatin with concurrent radiotherapy was found to be a safe and effective preoperative treatment. A complete resection was also feasible in highly selected stage IIIB patients.

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Combined analysis of apoptotic index and growth fraction in non-small cell lung carcinomas

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Purpose: To investigate the significance of apoptotic index (AI) and growth fraction in predicting survival of completely resected non-small cell lung carcinomas (NSCLC).

Methods: Sections of 89 NSCLC (27 adenocarcinomas and 62 squamous cell carcinomas) served for TUNEL staining to detect apoptotic cells and immunohistochemical staining to detect MIB-1 expression (i.e. growth fraction). The AI was defined as the number of apoptotic cells per 1,000 tumor cells. To evaluate the percentage of MIB-1 positive nuclei, 1,000 tumor cells were scored for each case. The postoperative survival rate according to AI and MIB-1 immunoreactivity was analyzed by the Kaplan-Meier method. Patients were excluded from survival calculations if death occurred within 30 days from surgery.

Results: The median AI was 11 (33rd-66th percentiles, 8-17). AI was significantly lower in adenocarcinomas (median 8) than in squamous cell carcinomas (median 13.5) (p=0.02). MIB-1 immunopattern was nuclear and the median value of MIB-1 staining was 30.4% (33rd-66th percentiles, 21.52-34.02%). Among histotypes, no significant difference in MIB-1 expression was observed (p=0.7).

Interestingly, when AI and growth fraction were analyzed separately no association with clinical outcomes was observed. On the contrary, combining together AI and MIB-1, the cases with low AI (<33rd percentile) and high MIB-1 (> 66th percentile) identified a group with a significantly poor prognosis (log-rank test, p=0.0007).

Conclusions: The balance between apoptosis and growth fraction seems to be prognostic in patients with NSCLC.

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Front line chemotherapy with four different schedules of gemcitabine and carboplatin in stage IV non-small cell lung cancer (NSCLC)

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Purpose: We designed a phase II study in order to evaluate the activity and the tolerability of the combination of Gemcitabine (G) + Carboplatin (C) as first line chemotherapy for metastatic NSCLC. Gemcitabine and Cisplatin (CDDP) exhibit synergist cytotoxicity against NSCLC. Carboplatin appears to be equally efficacious with a better toxicity profile. According to our lab's preclinical data on SCLC cell lines, we explored four different schedules of administration of G + C.

Methods: From September 1998 to December 2000, 88 chemo-naive stage IV NSCLC pts were randomized to receive the same dose of G (1000 mg/m2) and C (AUC5), but with different sequences. Pts were randomly assigned to arm A: G on days 1 and 8 with C on day 1, given 4 hours before G; arm B: same schedule but with C given 4 hours after G; arm C: G on days 1 and 8 with C on day 2; arm D: G on days 2 and 9 with C on day 1. Courses were repeated every 21 days. All of the pts had ECOG PS 0–1; 58% were adenocarcinomas; 77% males; median age was 64 years (33–75); the four arms were balanced for pts' characteristics.

Results: At present all of the pts are valuable for toxicity, 73 pts for response. According to standard analysis the overall response rate (RR) was 40% (29/73, 95% CI: 28.5–50.9%). Response rate arm by arm was: 55% in arm A, 25% in arm B, 30% in arm C, 37% in arm D. Toxicity was generally mild without significant difference in the four arm. Grade 3–4 neutropenia and thrombocitopenia occurred in 11% in 14% of pts, respectively. No pts required hospitalization for toxicity. Overall median duration of response was 6 mos (range 3–11). Overall median survival was 13 mos (range 7–26). One-year and 2-year survival is 54% and 17%, respectively.

Conclusion: G + C is an active and safe combination in stage IV NSCLC. Our data seem to indicate that C given before G produces better results. In view of its activity and tolerability this schedule could become the first line standard regimen for metastatic NSCLC.

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Correlation between C-ERBB-4 receptor expression and response to gemcitabine-cisplatin chemotherapy in non-small cell lung cancer

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Background: While the overexpression of c-erbB gene family in several malignancies is associated with poorer prognosis, the association between the expression of the cellular markers and the response to chemotherapy is not yet clear. In this study we investigated the expression of c-erbB-4 receptor in NSCLC and correlated it with the response to gemcitabine-cisplatin combination chemotherapy.

Patients and Methods: Forty-three NSCLC patients with histologically or cytologically proven disease were treated with gemcitabine-cisplatin combination chemotherapy. Immunohistochemical stains for c-erbB-4 receptor were performed in 20 cases on paraffin sections using the avidin-biotin-peroxidase method.

Results: Two patients achieved complete response (5%), and 16 achieved partial response (37%) yielding an overall objective response rate of 42%. Minimal response was observed in 7 patients (16%) and disease stabilization in 7%. Immunohistochemical stain was positive for the presence of c-erbB-4 receptor in 25% of patients, and negative in 75%. No response was documented in c-erbB-4 positive patients (0/5) while an objective response (complete, partial or minimal) was seen in 11/15 (73%) c-erbB-4 negative patients. Negative stain for c-erbB-4 significantly favored response to gemcitabine-cisplatin combination (p<0.01).

Conclusion: C-erbB-4 expression status showed no correlation with survival and cannot be accepted at this time as a guiding factor for therapeutic management. These interesting results deserve further evaluation in a large-scale prospective trial before treatment recommendations on the basis of c-erbB-4 presence can be finally made.

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Induction chemotherapy with taxol (T), cisplatin (C) and gemcitabine (G) and subsequent radiation therapy with or without concomitant taxol for stage III non small cell lung cancer (nsclc). a galician lung cancer group (GLGC) study

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Introduction: Combined thoracic radiation and chemotherapy has become the treatment of choice for unresectable stage III NSCLC. The GLCG commenced a phase II study for these patients (p), with a scheme of induction chemotherapy of TCG combination and if not surgery, followed by consolidation thoracic radiation therapy with (Group-1) or without (Gr-2) taxol, according to avaible capacity to administer the concomitant treatment.

Material and Methods: A total of 60 p with stage III NSCLC (except for pleural T4) were included: age 58.2 years (range 36-72); 4 F/56 M; ECOG 0/1 in 7/53 p; squamous/adeno/large cell carcinoma: 63.3%/18.3%/18.3%; 12 p (20%) stage IIIA and 48 p (80%) stage IIIB. The common TCG induction scheme is: T 125 mgr/m2/iv, C 50 mgr/m2/iv and G 1000 mgr/m2/iv on days 1 and 8 every 3 weeks through 3 cycles. If no surgery, consolidation treatment in Gr-1 consisted of radiation therapy (60Gys, 180 cGy/day) with