correlated with weight (r=0.50, p<0.001) and LBM (r=0.33, p=0.036) and net gain was observed with 1.5-2 cans/d. Similarly, E patients demonstrated positive correlations between increasing total protein intake (meals plus E) and both weight gain (r=0.52, p<0.001) and increased LBM (r=0.46, p=0.004). Such correlations were not observed in C patients. Increased plasma EPA levels were associated with LBM gain (r=0.51, p=0.001).

Conclusion: This study demonstrates that energy and protein dense supplements can stabilise weight in cancer cachexia. Furthermore, net gain of body weight and LBM can be achieved with adequate consumption (1.5-2 cans/d) of such a supplement when it is enriched specifically with n-3 fatty acids and antioxidants.

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91 ORAL

Does systemic chemotherapy prior to surgery increase the operative risk of a major hepatectomy ?

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The efficacy of systemic chemotherapy sometimes allows secondary resection of hepatic metastases. The potential hepatic toxicity of anticancer agents may influence the surgical procedure and the post-operative complications of a major hepatectomy. The objective of this study was to assess the impact of preoperative chemotherapy on liver function, the modalities of hepatic surgery, and on postoperative morbidity.

Patients and Methods: Pts without known chronic liver disease, treated by right or left hepatectomy in a curative intent for liver metastasis were analyzed retrospectively. Two groups of pts were compared: 44 non pretreated pts versus 42 pts treated by systemic chemotherapy within 6 months before surgery (median duration of chemotherapy = 6,7 months [extr 1-26]) for the following characteristics using a multivariate analysis: age, gender, body mass index, cancer primary site, number and size of the liver metastasis, existence and duration of preoperative chemotherapy, duration of operative procedure, duration of clamping of the hepatic pedicle, blood loss volume, liver function tests (ASAT, ASAT, ALP, GGT, bilirubine, prothrombin time (PT)) before and just after surgery, existence of postoperative complications and total duration of hospitalization].

Results: The 2 groups were well balanced for all the preoperative characteristics except for age which was statistically different (50 vs 58.7 years, p=0,0002). Preoperative liver function tests, preoperative PT, duration of hepatectomy, duration of clamping of the hepatic pedicle, blood loss volume, postoperative complications, and total duration of hospitalization were not different between the 2 groups. Only the postoperative PT was significantly lower in the pretreated group: 60% versus 49%, p = 0.0002. The duration of preoperative chemotherapy (< 6 mois versus > 6 mois) did not influence those results.

Conclusion: Preoperative systemic chemotherapy, even longer than 6 months, did not seem to have a deleterious effect on the surgical procedure and the post-operative complications of a major hepatectomy for liver metastasis, neither on postoperative morbidity despite macroscopic abnormalities of the liver parenchyma frequently described during surgery. Only the postoperative PT was significantly lower in case of preoperative chemotherapy, but this biologic feature had no impact in terms of post-operative complications.

Lung cancer I

92 ORAL

Cisplatin/gemcitabine (CG) vs cisplatin/gemcitabine/ vinorelbine (CGV) vs sequential doublets of gemcitabine/ vinorelbine followed by ifosfamide/vinorelbine (gv/Iv) in advanced non-small cell lung cancer (NSCLC): final results of a Spanish lung cancer group phase III trial (GEPC/98-02)

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The GECP/98-02 trial was designed to compare a cisplatin-based 3-drug combination vs non-cisplatin sequential doublets vs a cisplatin-based reference regimen in NSCLC. The chemotherapy regimens administered were: Arm A: cisplatin 100 mg/m2 d1 plus gemcitabine 1250 mg/m2 d1&8; Arm B: cisplatin 100 mg/m2 d1 plus gemcitabine 1000 mg/m2 d1&8 plus vinorelbine 25 mg/m2 d1&8 repeated every three weeks; Arm C: gemcitabine 1000 mg/m2 plus vinorelbine 30 mg/m2 d 1&8 for three cycles followed by ifosfamide 3 gr/m2 d1 plus vinorelbine 30 mg/m2 d1&8. Eligibility criteria were measurable stage IV (brain metastases eligible if asymptomatic) or stage IIIB (malignant pleural effusion) NSCLC and PS=0-2. 562 patients (pts) were included between September 1998 and August 2000. Median age 58 (32-76); PS 0-1: 84.2%, PS 2: 15.8%; Stage IV: 79%, Stage IIIB: 21%. The three arms were balanced for the main prognostic features. Response rates were: Arm A: 41%; Arm B: 40%; Arm C: 24.1%. With a follow-up of 12 months median survival was: Arm A: 40.8w (95% CI, 24.5-57.2); Arm B: 34.4 w (95% CI, 27.1-41.7); and Arm C: 44.8 w (95% CI, 31.8-57.9). Toxicities include, in Arms A, B, C, respectively: Grade 3-4 neutropenia 26.3%, 30.1%, and 18.5%, with neutropenic fever in 6.3%, 22.4% and 7.4%; Grade 3-4 thrombocytopenia 18.2%, 23.1% and 7.4%. Nausea and vomiting, neuropathy and renal toxicity were similar in the three arms. Final results will be presented in october 2001.

93 ORAL

Sequential versus concurrent chemo-radiation (RT-CT) in locally advanced non small cell lung cancer (NSCLC): A French randomized phase III trial of GLOT-GFPC (NPC 95-01 study)

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Recent results suggest that concurrent RT-CT is superior to sequential administration in stage III NSCLC. From 10/96 to 05/00, 212 patients (pts) presenting with unresectable locally advanced NSCLC, stage IIIAN2/IIIB, treated in 30 french centers, were randomized in a phase III trial between sequential RT-CT (arm A) and concurrent RT-CT (arm B). The mean age was 57 years (18–70), PS 0 in 110 pts, 1 in 95; stage IIIAN2: 50, stage IIIB: 156, with normal renal, cardiac, hepatic and hematologic function. In arm A pts received induction treatment: Cisplatin (C) 120 mg/m^2 on D 1, 29, 57 and Vinorelbine (V) 30 mg/m^2/d once a week from day 1 to 78 followed by a thoracic radiotherapy (TRT) delivering 66 Gy in 33 fractions, 5 days per week for 6.5 weeks. Pts in arm B, received the same TRT starting on D 1 with 2 concurrent cycles of C 20 mg/m^2/d and Etoposide 50 mg/m^2/d (d1–5 and d29–33), followed by C 80 mg/m^2/d, D78 and 106 and V 30 mg/m^2/d, once a week, D 78 to 127. The total dose of C was equivalent in both arms. Treatment arms were well-matched for baseline characteristics. Survival results are evaluable in 207 pts, toxicity (G3–4 WHO) in 178 pts (Table). Treatment was stopped for toxicity in 18.2% pts (arm A) and 22.3% (arm B). Six toxic deaths occurred in arm A, 10 in arm B.

	Neutropenia	esophagitis	pneumonitis	Median Survival	1-year Survival	2-year Survival
ARM A	88%	1%	1.4%	13.8 mo	56%	23%
ARM B	75%	19%	2.3%	15	56%	35%

This large, randomized study shows an acceptable feasibility, the toxicity of this aggressive regimen reflects the multi-institutional phase III approach; the results, especially in Arm B, compare favorably with other trials, with a clear trend in favor to concurrent RT-CT. An updated analysis will be presented at the meeting.

94 ORAL

Paclitaxel plus carboplatin versus paclitaxel plus gemcitabine in advanced NSCLC. Final results of a randomized phase III study

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Purpose of our multicenter trial was to compare the efficacy and toxicity of the non-platinum combination Paclitaxel (P) plus Carboplatin (C) to the commonly used combination Paclitaxel plus Gemcitabine (G) in advanced inoperable NSCLC.

Patients and Method: Since February 1998, 509 patients were enrolled in the study. Among them, 201 chemotherapy - naïve patients with his-

tologically confirmed NSCLC inoperable were evaluable for analysis. 249 (Group A) were randomized to receive P 200 mg/m^2 in 3 h infusion, day 1 plus C AUC = 6, day 1 and 252 (Group B) to receive P 200 mg/m^2 in 3 h infusion, day 1, plus G 1 gm/m^2 days 1, 8. In both groups the treatment was given every 3 weeks with standard premedication and antiemetics without growth factors Eligibility criteria included WHO performance status 0–2, documented inoperable stage IIIA, IIIB, IV, stable brain metastasis, no prior chemotherapy and adequate renal and hepatic function. Baseline demographics and tumor characteristics were well-matched in both groups. Dose intensity of P was 94% and 89% in groups A and B respectively whereas for G 89%.

Results: Response rate for pts in group A was 28% (2%CR, 26%PR) (95%CI 21–36) whereas in group B 35% (5%CR, 30%PR) (95%CI 29–44) P = 0.12. Median TTP was 6.1 months (95%CI 5.2–7.0) for group A and 5.8 months (95%CI 5.1–6.5) for group B (P = 0.35). The median survival time was 10.3 months (95% CI 8.8–11.8) in group A and 9.8 months (95% CI 8.0–11.7) in group B (P = 0.36). The 1-year survival was 40.5% and 41.5% for groups A and B whereas the 2-year survival was 17.4% and 16.4% respectively The best prognostic factor for response was PS: 0–1 (P = 0.004) whereas for median and 1-year survival: stage (P = 0.001), PS (P < 0.0001) and response (P < 0.0001). No toxic deaths were seen. G 3/4 neutropenia was seen in 15% in both groups, thrombocytopenia G 3/4 2% in group A and 1% in group B and anemia G 3/4 5% and 2% in groups A and B respectively. Neurotoxicity G 3 was noticed in 8% and 6% in groups A and B respectively

Conclusion: These final results indicate that both combinations are effective, equally active with comparable toxicity. At least, in this study, the non-platinum combination is neither more active nor less toxic in NSCLC.

95 ORAL

Fractionated thoracic radiotherapy gives better symptom relief in patients with non-small cell lung cancer

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Aims: To determine whether fractionated thoracic radiotherapy offers better symptom relief, quality of life or survival than single fraction treatment in patients with advanced non-small cell lung cancer.

Methods: Patients were randomised to 30 Gy in 10 daily fractions (F) to the chest or a 10 Gy single fraction (S). The principal endpoint was physician-assessed symptom score for cough, chest pain, dyspnoea, haemoptysis and dysphagia. Subsidiary endpoints were survival and quality of life. Symptom scores were compared using the Wilcoxon signed rank test.

Results: 148 patients were randomised into groups matched for age, gender, histology, performance status and initial total symptom score (TSS). Patients randomised to F had lower TSS at 1 month review (p = 0.014) or at 1 and 3 month review (p = 0.001). This group also had better scores at either review for dyspnoea (p = 0.010), chest pain (p = 0.014) and cough (p = 0.029). Overall, TSS improved following TRT in 28/60 assessable patients with S and 40/57 with F (χ^2 = 6.64, df = 1, p = 0.01). Median survival was 23 weeks with S and 28 weeks with F (p = 0.197). Patients treated with S had higher anxiety scores than patients with F (1 month p = 0.01, 1 or 3 months p = 0.003).

Conclusions: Fractionated TRT offered better symptom relief and reduced anxiety compared to single fraction palliation, but did not increase survival.

96 ORAL

Postoperative oral administration of UFT for completely resected pathologic stage I non-small cell lung cancer: the West Japan study group for lung cancer surgery (WJSG), the 4th study

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[Purpose] To examine the efficacy of UFT, an oral 5-fluorouracil derivative anti-tumor agent, as a postoperative adjuvant therapy for p-stage I non-small cell lung cancer (NSCLC), because previous prospective studies suggested the efficacy for early-stage NSCCL patients. [Patients and Methods] Patients who underwent complete tumor resection with mediastinal dissection for p-stage I, adenocarcinoma (Ad) or squamous cell carcinoma (Sq) were eligible. A total of 332 patients were randomized to the surgery-alone group (control group) and the treatment group (UFT 400mg/m2 for 1 year after surgery, UFT group) after stratified by the histologic types. [Results] For Ad patients, the 5- and 8-year survival of the UFT group (n=120) were 85.2 and 79.5%, respectively, which seemed better than those of the control group (n=121) (79.2 and 64.0%, respectively) although without statistical significance (p=0.081). For p-stage IA Ad patients, the difference reached statistical significance (p=0.011). For Sq patients, there was no difference in the prognosis between the control group (n=48) and the UFT group (n=43). For all p-stage IA NSCLC patients, the 5- and 8-year survival rates of the UFT group were 85.8 and 79.7%, respectively, significantly better than those of the control group (76.7 and 61.6%, respectively, p=0.027). In contrast, UFT proved not to be effective for p-stage IB NSCLC patients. [Conclusions] Postoperative UFT administration proved to be effective for p-stage IA NSCLC patients, especially for p-stage IA, Ad patients.

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A three-arms phase III randomised trial comparing combinations of platinum derivatives, ifosfamide and/or gemcitabine in stage IV non-small cell lung cancer (NSCLC): an european lung cancer working party study

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Purpose: To determine, in stage IV NSCLC, if the combination of gemcitabine -a new active drug - with ifosfamide (IG) or with the cisplatin-carboplatin association (CCG) will improve survival (primary endpoint) in comparison to a first-generation regimen, cisplatin-carboplatin-ifosfamide (CCI).

Patients and methods: A total of 284 patients without prior chemotherapy and with metastatic NSCLC were randomised. Four were ineligible and 16 not assessable for responses. Cisplatin was given at 60 mg/m2 on day 1, carboplatin AUC 3 on day 1, ifosfamide 4.5 g/m2 on day 1 and gemcitabine lg/m2 on days 1,8 and 15. Courses were repeated every 4 weeks. Response was assessed after 3 courses and chemotherapy was continued in case of response until best response. There were 94 eligible patients in the CCI arm, 92 in CCG and 94 in IG.

Results: Objective response rate was, respectively for CCI, CCG, and IG, 23% (95% CI: 15-32), 29% (95% CI: 20-39) and 25% (95% CI: 16-33) (p = 0.61). Median survival time was respectively 24,34 and 30 weeks (p = 0.20); 1-year survival time 23%, 33% and 35% and 2-year survival time was 11%, 14% and 17% respectively. There was a significant survival advantage in disfavour of CCI in the subgroups of women and of patients older than 60 years. Toxicity was tolerable: severe alopecia was less frequent in the CCG arm, IG was significantly associated with more thrombopenia and CCG with more leucopenia.

Conclusion: The regimens including a new drug (gemcitabine) were associated with a better survival (statistically significant in some subgroups) than a classical first-generation cisplatin containing regimen in the treatment of stage IV NSCLC. The non-platinum combination with gemcitabine was as effective as the platinum regimen with gemcitabine.

98 ORAL

Phase II Eastern Cooperative Oncology Group (ECOG) pilot study of paclitaxel (P), carboplatin (C), and trastuzumab (T) in HER-2/neu (+) advanced non-small cell lung cancer (nsclc): early analysis of e2598

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Background: Multiple NSCLC cell lines and 20% to 50% of pathologic specimens express HER-2/neu, the target of trastuzumab (Tsai JNCI 1993;85:897). HER-2/neu expression has also proven to be an independent, unfavorable prognostic factor in resected patients with pulmonary adenocarcinoma (Cancer Res 1990;50:5184-91). Trastuzumab has demonstrated in vitro synergy with carboplatin and additivity with paclitaxel. ECOG therefore launched a phase II study evaluating combination carboplatin, paclitaxel and trastuzumab in patients with incurable, advanced NSCLC.

Methods: Eligibility stipulated measurable tumor; HER-2/neu positivity (1+ to 3+ by IHC, confirmed by central pathology review); ECOG PS 0-1;