at a dose of 225 mg/m2 administered over 3 hours, of the same P combined with C at an AUC of 6, both administered on day 1 and repeated every 3 weeks to a maximum of 6 cycles. QoL was assessed by the EORTC C-30 and EORTC Lung Module questionnaires, in addition to utility assessment forms. A total of 584 pts were accrued from 10/97 to 12/00. Median age 64, M/F: 399/185, PS 0–1/2: 485/99. Toxicities (Gr 3/4) included:

	P [N = 267] (%)	CP [N = 268] (%)
ANC	32	62
PLT	1	11
HGB	3	13
Febrile neutropenia	5	8
N/V	3	8
Dyspnea	7	6
Peripheral neuropathy	12	13
At least one grade 3/4 toxicity	70	90
Toxic death	<1	<1

Response and survival data will be mature as of September 2001 and will be available for an original presentation at the time of the meeting. Preliminary QoL data will also be presented.

560 ORAL

Cisplatin and gemcitabine combined with herceptin in patients (pt) with her2 overexpressing, untreated, advanced, non-small-cell lung cancer (NSCLC): a phase II trial

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Herceptin has been shown to be synergistic with cisplatin and gemcitabine in NSCLC with HER2 overexpressing. We studied Herceptin plus gemcitabine/cisplatin in HER2 overexpressing advanced NSCLC pts. Eligibility was, zubrod <2, chemonaive stage IIIB/IV, ejection fraction (EF) >40%, >1+HER2 by immunohistochemistry (IHC) (DAKO, HercepTest®) or >15ng/ml serum HER2 shed antigen by (ELISA) (Oncogene Science®). Treatment was Herceptin 2mg/kg/wk IV, gemcitabine 1250mg/m2 IV d1/d8, cisplatin 75mg/m2 IV d1 every 3weeks x 6 followed by maintenance Herceptin 2m/kg/wk IV until progression. 76 pts had both IHC and ELISA. By ELISA, 13/76(17%) pts >15ng/ml of whom 6/13(46%) had IHC >1+. By IHC, 18/76(24%) pts >1+ of whom 6/18(33%) had ELISA >15ng/ml. Pharmacokinetics on 7 pts showed no differences in clearance (paired t-test) of gemcitabine when given with cisplatin versus this study's internal control; cisplatin/Herceptin. At present, 12/14(86%) pts are evaluable for response. Median age 60 (range 46-69), gender, 8 females/4 males. No pts had EF decrease by >10% or below <40%. Grade 3 toxicities: neutropenia 6/12(50%), thrombocytopenia 5/12(42%), anemia 2/12(17%), fatigue 2/12(17%), nausea 1/12(8%). Grade 4: neutropenia 4/12(33%). During maintenance, there was no toxicity >grade 1. Responses are as follows: partial response 6/12(50%), stable disease 5/12(42%), progression 1/12(8%). There are 4/12(33%) pts still receiving chemotherapy/Herceptin. Maintenance was begun on 7/12(58%) and durations were 8-50+ weeks. We conclude that this regimen is well tolerated and response rates are encouraging. Herceptin does not alter gemcitabine clearance. Elevated expression by HER2 IHC is associated with increased serum antigen titers. Since maintenance Herceptin causes minimal toxicity with prolonged treatment, time to progression and survival will be critical endpoints.

561 ORAL

An EORTC randomized phase III trial of three chemotherapy regimens in advanced non-small cell lung cancer

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EORTC 08975 was designed to compare the standard arm cisplatin (P)-paclitaxel (T) (T 175 mg/m2/3h dl + P 80 mg/m2 dl) with cisplatin-gemcitabine (G) (G 1250 mg/m2 d 1, 8 + P 80 mg/m2 dl) and the non-cisplatin-based regimen of T 175/mg/m2/3 hrs d1 + G 1250 mg/m2 d1, 8. All 3 schedules were repeated every 21 days. Eligible patients (pts) were required to have measurable disease; PS = 0-2; and Stage IIIB (malignant pleural effusion and/or supraclavicular nodes) or Stage IV. 480 pts were randomized between 8/98 and 7/00 (T+P 159; G+P 160; T+G 161; PS0=27%; PS1=61%; PS2=12%; IIIB=21%, IV=79%; squamous cell=24%, adeno=41%; undiff=31%; other 4%). In general, the 3 regimens were well tolerated. Gr 4 thrombocytopenia was more common with G+P (table).

Worst toxicities (NCIC) (in evaluated pts)	T+P	G+P	T+G
Gr 4 ANC %	8.8	10.6	8.1
Gr 4 thrombocytopenia %	0.6	11.3	1.9
Gr 3 nausea %	6.3	9.4	3.1
Gr 3 vomiting %	5.0	8.1	3.1
Gr 3 sensory neurotoxicity %	2.5	0.6	0.0
Gr 3 febrile neutropenia %	1.9	2.5	1.2
Worst gr 4-5 %	7.5	8.8	8.1
N of toxic deaths	2	0	4

Severe nausea/vomiting were least common in arm T+G and sensory neuropathy in arm T+P. At the time of the 04/00 analysis, 354 of the 369 deaths needed for final analysis have occurred. The response rate & survival results of the individual arms will be available for presentation October 2001.

562 ORAL

Docetaxel + Cisplatin (DC) and Docetaxel + Carboplatin (DCb) vs Vinorelbine + Cisplatin (VC) in chemotherapy-naïve patients with advanced and metastatic non-small cell lung cancer (NSCLC): Results of a multicenter, randomized phase III study

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Purpose: To compare the safety and efficacy of DC or DCb with the 'reference' regimen VC in chemotherapy-naïve patients with unresectable locally advanced and/or recurrent (Stage IIIB) or metastatic (Stage IV) NSCLC.

Methods: This open-label, parallel-group, randomized study enrolled 1220 patients from 140 sites in 29 countries. Patients received: DC (D 75 mg/m^2 1 h iv followed by C 75 mg/m^2 iv q3wk); DCb (D 75 mg/m^2 1 h iv followed by Cb AUC = 6 q3wk); or VC (V 25 mg/m^2/wk and C 100 mg/m^2 iv q4wk). 67% of the patients were metastatic and 96% had KPS $\geq$ 80.

Results: Overall survival was significantly better with DC vs VC ($p = 0.0469$). Survival rates with DC and VC were 47% and 42% at 1 year, and 21% and 14% ($p = 0.035$) at 2 years. Median survival was 10.9 mouths with DC vs 10 months with VC. Overall survival with DCb was non-inferior to VC (hazard ratio = 1.046; 95% CI, 0.891–1.227). Survival rates with DCb and VC were 38% and 42% at 1 year, and 16% and 14% at 2 years. The median with DCb was 9.1 months vs 10.0 months with VC. More patients in the VC arm experiencered Grade 3/4 anemia (24%) compared with the DC (7%) or DCb (10%) arms ($p < 0.01$). There was no significant difference in the number of patients in any arm who experienced Grade 3/4 neutropenia, thrombocytopenia, infection or febrile neutropenia. Use of prophylactic antibiotics or G-CSF was similar in all arms. More patients in the VC arm experienced Grade 3/4 nausea (16%) and vomiting (16%) compared with the DC (10% and 8%) or DCb (6% and 5%) arms ($p < 0.01$).

Conclusion: This is the first Phase III study showing an overall survival advantage for a docetaxel + cisplatin regimen compared with a standard doublet in the first-line treatment of advanced NSCLC. Docetaxel + platinum regimens were associated with significantly less Grade 3/4 nausea, vomiting and anemia compared with VC. These results indicate that docetaxel + platinum combinations are safe and effective first-line options in NSCLC.