Methods: From 9/96 to 2/99, 79 previously untreated pts received either TP (Taxol 200 mg/m^2, Cisplatin 80 mg/m^2 d1) or EP (Etoposide 100 mg/m^2 d 1–3, Cisplatin 80 mg/m^2 on d1) q3wks. St IIIB pts had 3 cycles (cyc) followed by RT at 60 Gy; st. IV up to 6 cyc (less if progressive disease).

Results: 84% males; age 56 [34–68]; WHO PS 0&1 in 45, 2 in 34 pts; histology (H): squamous 52, adeno 15, large cell 8, mixed 4 pts; AJCC st: IIIB 50, IV 29 pts; TP 32, EP 47 pts. **Toxicity** (tox): 256 cyc were given, with one toxic death in EP arm (renal failure). Gr. 4 haematological tox was rare (neutropenia 7, anaemia 1 cyc, in both arms). Gr. 1 neurological and cardiac tox occurred in 4 and 1 TP pts, respectively. **Activity:** 29 pts had an objective response (OR) to CT (= 37%, CI [26%–47%]), 4 CR, 25 PR. Response rate was influenced by the PS (0–1 vs 2: 49% vs 21%, $p < 0.01$) and weight loss ($\leq$5% vs $>$ 5%: 45% vs 17%, $p < 0.02$). Factors not significant for OR: protocol TP vs EP, stage, sex, age, H. **Survival** (S): at a median follow-up of 8 months (m) [1–23], median S is 7.5 m; 9 vs 7 m for st IIIB vs st IV pts ($p < 0.03$); 10 vs 6.5 m for CT responders vs refractory pts ($p < 0.01$). A trend existed in favour of TP (median S – TP vs EP: 9 vs 7 m, 1-year S 34% vs 14%), but not statistically significant. S was not influenced by sex, age, PS, weight loss or H. To date, 27 pts are alive and 52 have died: 49 pts disease progression, 1 trt complication, 2 other causes.

Conclusions: 1) TP and EP were equally active in advanced NSCLC pts (OR 38% vs 36%). 2) There was a trend towards improved S with TP. 3) Prognostic factors found: for response – PS and weight loss; for survival-stage and response to CT.

999 POSTER

A multicenter phase II trial with gemcitabine (GEM) and vinorelbine (VNR) in the treatment of non-small cell lung cancer (NSCLC) stage IIIB and IV

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Purpose: To evaluate the efficacy and safety of a combination with GEM and VNR in the first line treatment of advanced NSCLC.

Methods: Patients (pts) with NSCLC stage IIIB or IV received GEM 1000 mg/m^2 and VNR 30 mg/m^2 on days 1, 8, 15, every 4 weeks to a maximum of 8 courses. GEM was given over a 30-min infusion followed one hour later by VNR (15-min infusion). The doses of GEM and VNR were modified as follow: neutrophils $>$ 1.5/nl and platelets $>$ 100: no reduction, neutrophils 1.0–1.49/nl or platelets-75–99/nl: 50% dose reduction, neutrophils $<$ 1.0/nl or platelets $<$ 75/nl: delay.

Results: Between Dec 1997 and Nov 1998 70 pts with KPS 70–100% were enrolled. We can present preliminary data of 62 pts (study on going): 12.9% stage IIIB/87.1% stage IV; 48 male/14 female; mean age 58.6 (range 38–74). Histologic types: adenocarcinoma 40.3%, squamous cell carcinoma 27.4%, large cell carcinoma 24.2% and other classified NSCLC 8.1%. 50 pts were evaluable for response and 56 pts for toxicity. The overall response rate (ORR) was 46%. 1 CR (2%), 22 PR (44%), 13 SD (26%), 14 PD (28%). 174 cycles of chemotherapy were given. Toxicity (WHO): leukopenia G 3: 14.9% and G 4: 6.9%, thrombocytopenia G 3: 1.7% and G 4: 0.6%, anemia G 4: 1.7% of cycles. 3.6% of 56 pts presented G 2 and 5.4% G 3 peripheral neurotoxicity, 14.3% G 2/5.4% G 3 local phlebitis, 10.7% G3 infections, 5.4% G2/5.4% G3 reactions of skin, 3.6% G 3 vomitus/emesis, 5.4% G 3 pulmonary toxicity, 1.8% G 3/1.8% G 4 constipation, 5.4% G 2/5.4% G 3 mucositis, 3.6% G 3 increase of transaminases, 1.8% G 3 alopecia. 28 (16.1%) reductions of doses and 38 (21.8%) delays occurred in the administration of GEM and VNR.

Conclusions: These preliminary results suggest that the combination of GEM and VNR has major antitumor efficacy in advanced NSCLC with manageable toxicity. Although the sequence of drugs applied remains obscure, we believe that our sequence contributed to the comparatively high response rate. In summer 1999 we will start a multicenter randomized phase III study (GEM + VNR vs GEM + VNR + CDDP) in Germany to investigate the role of cisplatin. To avoid hematological toxicities GEM and VNR will be given on days 1 and 8 within 3-weeks cycles.

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Raltitrexed ('Tomudex') and oxaliplatin: An active out-patient regimen in malignant mesothelioma

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Introduction: A previous Phase I study showed that a combination of raltitrexed ('Tomudex') and oxaliplatin appeared to yield some activity in both pre-treated and chemotherapy-naive mesothelioma patients (pts) [Fizazi et al, ASCO 1998]. The aim of this Phase II study was to further evaluate the activity of this combination in malignant mesothelioma. We present validated results from the first 23 pts.

Methods: Raltitrexed 3 mg/m[2] was given by a 15-min iv infusion followed 45-min later by oxaliplatin 130 mg/m[2] 2-h iv infusion repeated every 3 weeks.

Results: 50 pts (37 M/13 F) with a median age of 59 (range 43–74) yrs, and a WHO performance status of 0 (12 pts), 1 (27 pts) or 2 (11 pts) have been entered. 11 pts were pre-treated with platinum-based chemotherapy and 39 were chemotherapy naive. Among the 23 pts fully evaluable for safety, the following toxicities (NCI-CTC grade II and above) were recorded: grade II anaemia (3 pts), neutropenia (1 pt), vomiting (3 pts), nausea (2 pts), paresthesia (3 pts) and asthenia (12 pts), and grade III asthenia (2 pts), neutropenia (1 pt) and diarrhoea (1 pt). Response (WHO criteria) imaging evidence has been reviewed by an external panel. 21 pts are evaluable for efficacy (2 pts are ineligible due to the absence of measurable disease) and, of these, a partial response was seen in 6 pts (28.6% [95% CI 9.2–47.9]), stable disease (including 6 minor responses) in 11 pts (52.4%), and progressive disease in 4 pts (19%). Among the 16 evaluable chemotherapy-naive pts, 5 achieved partial response (31.3%), 8 had stable disease (50%) and 3 progressed (18.7%). In the pre-treated population, 1 partial response was seen in a cisplatin-refractory patient, 3 pts had stable disease and 1 pt progressed.

Conclusion: This preliminary activity/toxicity report shows that raltitrexed plus oxaliplatin has an acceptable tolerability profile and is active in malignant mesothelioma. Accrual is ongoing.

'Tomudex' is a trade mark, the property of Zeneca Ltd.

1001 POSTER

Cisplatin – Paclitaxel – Topotecan (CPT) weekly administration in chemo-naive or pretreated extensive disease small cell lung cancer (ED-SCLC). A SICOG Phase II study

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Purpose: To define the antitumor activity of the CPT weekly administration with G-CSF support in chemo-naive or pretreated SCLC pts with extensive disease.

Methods: Pretreated or chemo-naive patients with ED-SCLC received Cisplatin 40 mg/m^2, Paclitaxel 85 mg/m^2 and Topotecan 2.25 mg/m^2 weekly, with filgrastim (5 μgr/kg d 3–5) support. A minimum of 6 weekly cycles were delivered. In presence of major response additional 6 cycles were given.

Results: To date, 26 ED-SCLC patients (20 chemonaive, 6 pretreated) have been treated, for a total of 158 cycles delivered. The treatment was generally well tolerated. Grade 4 neutropenia and thrombocytopenia occurred in 3 and 1 pts, respectively. Anemia was more frequent and 3 blood transfusions were required. Severe diarrhoea, parhestesias and fatigue occurred 6, 2 and 8 pts, respectively. At the present analysis 18 chemo-naive and 5 pretreated pts are evaluable for response. 3 CRs and 10 PRs have been recorded in chemo-naive pts for a 72% ORR. One complete and 2 partial responses have occurred in the 5 evaluable pretreated pts. At a 7 (1–16)-month median follow-up only 3 deaths have occurred.

Conclusions: The weekly CPT combination with G-CSF support represents a well tolerated therapeutical approach either in chemo-naive or pretreated ED-SCLC pts. The activity rate in chemo-naive pts. seems at least similar to that achievable with the standard front-line approaches. The study continues until the planned final sample size of 53 pts.