Significantly longer survival in pts treated with surgery was found in all T and N categories except N2 disease. Local relapse was more frequent in pts treated conventionally (55%) then in surgically (15%, p<0.001). Distant relapse rates were similar in both groups (36% and 40%, respectively). The most common site of metastases in the entire series was CNS followed by liver, lymph nodes, bones, lungs and skin.

We conclude, that surgery may have a positive impact on survival of LD SCLC pts, and a randomized study addressing this issue should be considered.

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Randomized, phase II study of topotecan/paclitaxel versus cisplatin/etoposide in patients with untreated, extensive disease, small cell lung cancer (SCLC)

H. Lena[1], J. Breton[2], W. Yu[3], K. Steppert[4], K. Lightcap[5], G. Ross[5], M. Lymboura[5]. [1] *Hospital Pontchaillou, Rennes, France;* [2] *Centre Hospitalier de Belfort, Belfort, France;* [3] *Princess Margaret Hospital, Kowloon, Hong Kong;* [4] *Bezirksklinikum Kutzenberg, Ebensfeld, Germany;* [5] *GlaxoSmithKline, Oaks, USA*

Topotecan and paclitaxel are active single agents in the treatment of SCLC. In previous phase II studies, the combination of topotecan and paclitaxel has demonstrated encouraging activity, suggesting that this combination is worthy of further investigation. This phase II study was designed to compare the combination of topotecan (T) and paclitaxel (Px) with the standard front-line therapy of cisplatin (P) and etoposide (E). Eligible patients had bidimensionally measurable disease, ECOG PS 0-2, and adequate bone marrow, hepatic and renal function. Asymptomatic brain metastases were allowed. Recruitment is completed with 151 patients randomized (76 on the TPx arm and 75 on the PE arm), and preliminary results are pending. Demographic baseline characteristics: females/males 36/115; median age 61; median PS=1; elevated LDH 66%. Patients were randomized to receive either TPx: T 1.0 mg/m2/d IV d 1-5 and Px 175 mg/m2 IV d 1 with prophylactic G-CSF 5ug/kg/d SC starting d 6 for all patients; or EP: P 80 mg/m2 IV d 1 with E 100-120 mg/m2 IV d 1-3. Cycles were repeated every 21 days. The primary efficacy variable is objective response rate, which is to be verified by independent, blinded radiologic review.

Response and tolerability data will be available by the time of the meeting.

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Cisplatin-epirubicin-paclitaxel (PET) weekly administration with G-CSF support in extensive SCLC. A SICOG phase II study

N. Panza, G. Frasci, G.P. Nicolella, P. Comella, L. Maiorino, D. Muci, A. Farris, A. Lamberti, E. Barbato, G. Comella. *SICOG c/o INT, Naples, Italy*

Background: In a previous phase I study (Frasci et al. Br J Cancer 2001 in press) we showed that cisplatin 40 mg/sqm, paclitaxel 85 mg/sqm and topotecan 2.25 mg/sqm could be safely given weekly in presence of G-CSF support, and that an 80% ORR can be achieved in advanced disease with this regimen.

Purpose: We tried to improve the efficacy of the treatment by increasing the dose of paclitaxel (from 85 to 120 mg/m2), and replacing topotecan with epirubicin (50 mg/m2/week). The dose of cisplatin was slightly decreased to 30 mg/m2/week. This regimen at the present doses had already been tested in a large number of breast cancer patients.

Patients and Methods: Patients with extensive SCLC, aged 18-70, with ECOG PS < 2 were considered eligible provided that they had not received prior chemotherapy. They received weekly P, E, and T at the above reported doses for a maximum of 12 cycles. G-CSF was given on days 3-5 of each week. The planned final sample size was of 33 patients, calculated according to the Simon two-stage design (end point was considered the CR, with a p1=30% and p0=10%), but a preliminary analysis was planned after 22 patients.

Results: As of April 9, 2001, 24 patients have been included in the study (median age 61; PS 0-1/2=13/11) for a total of 178 weekly cycles delivered. Twenty-three patients have been considered eligible for toxicity and response since in one case the hystotype resulted to be NSCLC after a careful revision.

Overall, grade 3-4 neutropenia and thrombocytopenia occurred in 7 and 3 patients. One patients died after 1 cycle due to cardiac failure probably related to sepsis. Anemia was the most frequent hematologic side effect, 9 patients requiring at least once red blood cell transfusions. Symptomatic thrombocytopenia was never observed. Nonhematologic side effects were in general moderate. Severe emesis, mild peripheral neuropathy and severe fatigue were observed in 2, 8, and 5 patients respectively. Among the 19 patients who completed at least 6 cycles 5 complete responses and 10 partial responses have been recorded for a 79% ORR [95% CI=54-94].

Conclusions: The cisplatin, epirubicin, paclitaxel regimen is well tolerated and highly active in extensive SCLC patients. The accrual continues until the planned sample size of 33 patients is reached.

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Activity of ZD0473 in small-cell lung cancer: an update in patients relapsing after one prior chemotherapy regimen

J. Schiller[1], P. Bonomi[2], M. Modiano[3], P. Cornett[4], M. Koehler[5]. [1] *University of Wisconsin Comprehensive Cancer Center, Madison, USA;* [2] *Rush-Presbyterian-St-Luke's Medical Center, Chicago, USA;* [3] *Arizona Clinical Research Center, Tucson, USA;* [4] *Veterans Affairs Medical Center, San Francisco, USA;* [5] *AstraZeneca, Wilmington, USA*

Aims: This Phase II multicenter study was conducted to assess the use of the new generation platinum drug, ZD0473, in patients with small-cell lung cancer who have previously failed one platinum-based chemotherapy regimen.

Methods: ZD0473 (120-150 mg/m2) was administered by a 1-h intravenous infusion on day 1 of each 3-week cycle. Patients were evaluated in two cohorts: (1) drug resistant (relapsed or progressed ≤8 weeks following prior chemotherapy); and (2) sensitive (relapsed or progressed beyond 8 weeks).

Results: In this ongoing trial, 38 patients with a median age of 62 years (range 38-80) have been recruited at present (F:M [15:23 patients]; resistant:sensitive [11:27]; performance status 0-1 [33] and 2 [5]). To date, 93 treatment cycles have been administered: median 2 cycles per patient (range 1-6), with 9 patients receiving ~4 cycles. Overall, 52 cycles were completed without dose reduction or delay, 12 cycles required dose reduction of >20%, and 13 cycles had a delay of ~7 days. Grade 3 or 4 hematologic toxicities (Common Toxicity Criteria) included thrombocytopenia (grade 3 [7 patients]; grade 4 [9]) and neutropenia (grade 3 [7]; grade 4 [1]). The most frequent grade 3 or 4 non-hematologic event was dyspnea (grade 3 [4]), irrespective of causality. Two patients withdrew due to hematologic toxicity. Response to treatment was evaluable in 6 resistant patients: 1 patient had a partial response and 5 patients had progressive disease. Of 21 evaluable sensitive patients, 2 patients had a partial response, 11 had stable disease (including 6 with some evidence of tumor shrinkage) and 8 had disease progression. Across the entire study population, 7 patients had an improvement in WHO score at endpoint. To date, 10 of 25 patients have died due to disease progression. Updated survival data will be presented.

Conclusion: ZD0473 had a manageable tolerability profile and there was a favorable response to treatment in terms of tumor response and stable disease, in both platinum-sensitive and -resistant patients.

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Paclitaxel and Gemcitabine for refractory or relapsed small cell lung cancer (SCLC). A multicentric phase II study

M. Domine[1], J. Gonzalez Larriba[1], R. Garcia Gomez[1], S. Morales[2], D. Isla[2], C. Garcia Giron[3], I. Maestu[3], V. Giner[4], S. Terrasa, J. Andrade[4], R. Alfonso, F. Lobo [5]. [1] *Fundacion Jimenez Diaz, Hospital Clinico, Hospital Gregorio Marañon, Oncologia, Madrid, Spain;* [2] *Hospital Arnau de Vilanova, Lleida, Hospital Clinico, Oncologia, Zaragoza, Spain;* [3] *Hospital General Yague, Burgos, Hospital Virgen de los Lirios, Oncologia, Alcoy, Spain;* [4] *Hospital Sagunto, Hospital Son Dureta, MallorcaHospital Virgen Salud, Oncologia, Toledo, Spain;* [5] *Hospital Clinico, Universitario Fundacion Jimenez DÃaz, Oncologia, Madrid, Spain*

Paclitaxel and gemcitabine have shown activity in SCLC, as single agent or in combination with others drugs, in untreated and even pretreated patients. Paclitaxel ® gemcitabine seems to be an attractive combination to explore in SCLC. We conducted a prospective phase II study to determine the activity of this combination as second line treatment in SCLC.

Patients and Methods: Patients were eligible if they had measurable or evaluable disease, performance status (ECOG) 0-2 and adequate hepatic, renal and bone marrow function. Paclitaxel dose was 175 mg/m2 (3 hour infusion)on day 1 and gemcitabine 1250 mg/m2 (30 minute infusion)on days 1 and 8. Cycles were administered every 3 weeks.

Results: 41 pts were enrolled, 37 male and 4 female. Median age was 62 years (range 42- 79); 83% had PS 0 or 1 and 17% PS 2; 17 pts had refractory disease (defined as progression within 3 months of starting