IV 38.2% vs 34.4%, operable pts 35% vs 31% respectively in Y.P. and E.P. Surgery, however, was performed in 73 (28.7%) Y.P. and in only 6 (18.8%) E.P.. Chemotherapy (CT) consisted of 6 courses of alternating CAV/PE for extensive disease pts.. LD pts were treated with 4 cycles of CT plus surgery in operable pts; RT (44 Gy) followed CT in inoperable pts. Two pts had an early death before starting treatment, 3 pts were submitted only to surgery for refusal of CT, all in Y.P. group. In 44 pts surgery was followed by adjuvant CT. A total of 237 pts were submitted to primary CT, 210 pts were Y.P., 27 E.P.: objective response rates were 72% and 63% respectively, with 26.7% (56 pts.) and 22.2% (6 pts.) CR. Median survival was 11.6 and 12 months and 3 yrs survivals were 18% and 17.8%. Cox proportional hazard survival analysis showed no significant differences by age. *Conclusions:* compliance, responses and survival were similar in Y.P. and E.P. treated for SCLC. Thus an aggressive therapeutical approach seems to be justified in selected patients older than 70 yrs.

83 ORAL

PROPHYLACTIC CRANIAL IRRADIATION (PCI) FOR PATIENTS (PTS) WITH SMALL CELL LUNG CANCER (SCLC) IN COMPLETE REMISSION (CR)

R. Arriagada, I. Monnet, A. Rivière, J.A. Santos-Miranda, E. Bardet, A. Laplanche, the PCI85-PCI88 trialists
Coordinating center: Institut Gustave-Roussy, Villejuif, France

Two randomized trials were planned to evaluate the effect of PCI (24 Gy/8 fractions/12 days) on brain metastasis (brmet), overall survival (OS) and late toxicity rates in pts. with SCLC in CR. The first trial (PCI85) included 294 evaluable pts. and showed that PCI decreased the risk of brmet 3-fold without a significant increase in complications. A possible beneficial effect on overall survival was not statistically significant ($P = 0.14$). The second trial (PCI88) was started in 1988 with a simplified schedule to increase pt accrual and the statistical power so that a potentially beneficial effect on overall survival would be detected. This trial included 211 pts and was closed in April 1994. In the two trials, 505 pts. are evaluable, 418 with limited disease and the median follow-up was 63 months. Only one pt. was lost to follow-up. Overall results are summarized as follows:

	2-year rates				
Endpoint	PCI(+)	PCI(−)	RR	(IC)	p Value
Overall brmet	40%	59%	0.45	(0.34–0.60)	$<10^{-4}$
Isolated brmet	39%	57%	0.41	(0.30–0.57)	$<10^{-4}$
OS	31%	27%	0.85	(0.69–1.03)	0.10

In conclusion, the effect of PCI on overall survival in pts with SCLC in CR was not statistically significant. A meta-analysis of similar trials should be conducted to evaluate a possible beneficial effect of PCI.

84 ORAL

PHASE II STUDY OF TOPOTECAN IN REFRACTORY AND SENSITIVE SMALL CELL LUNG CANCER (SCLC)

A. Ardizzoni, H.H. Hansen, P. Dombernowsky, S. Kaplan, P.E. Postmus, T. Gamucci, B. Schaefer, J. Wanders, J. Verweij
EORTC-ECTG and EORTC-LCCG

Topotecan (T) is a semisynthetic-camptothecin analog with specific topoisomerase I inhibitory effect and preclinical activity in a broad range of tumors including SCLC. A multicentre Phase II study to assess activity and toxicity in pretreated SCLC patients (pts) has recently been closed. Two groups of pts were enrolled: "sensitive" (S) pts who responded to 1st line chemotherapy (CT) but progressed <3 months afterwards and "refractory" (R) pts who never responded to 1st line CT or progressed <3 months after 1st line CT. T was administered iv at a dose of 1.5 mg/m^2 d×5 q3 weeks until progression or excessive toxicity. A total of 94 eligible pts were entered and 353 courses (crs) and 87 pts (48 R, 39 S) have been evaluated. Pts characteristics are: median age 59, median PS 1, median duration of prior CT 4 months and median No. of prior drugs 3. In 39 S pts 5 CR and 13 PR were observed (46%), in 48 R pts 1 CR and 3 PR (8%). Toxicity (NCI grading) was mainly hematological. Leucopenia, although short-lived was common with gr. III and IV neutropenia occurring in 78% of crs. Nine pts developed infections, 2 died while neutropenic. Gr. III and IV thrombocytopenia was observed in 29% of crs and 54% of pts. Anemia gr. III and IV occurred in 29% of pts. Non-hematological toxicity was mild. Asthenia was observed in 35% of crs with only 3 gr. IV episodes. Diarrhea was reported in 12 crs (1 gr. III), vomiting gr. III in only 1 crs. Toxicity required dose reduction in 10% of courses, treatment delay in 18% of crs. Preliminary results indicate that the concept of testing new drugs in S and R pts is feasible, that T has significant activity, especially in S, but even in R pts, and that toxicity is manageable. The study is closed for patient entry and final results will be available in October 1995.

85 POSTER

A PROSPECTIVE RANDOMISED STUDY IN LIMITED DISEASE SMALL CELL CARCINOMA—DOXORUBICIN AND VINCRISTINE PLUS EITHER CYCLOPHOSPHAMIDE OR ETOPOSIDE

R.P. Abratt[1], P.A. Willcox[2], D.G.M. Salton[3], J.R. Malan[4]
[1] Department of Radiation Oncology
[2] Department of Respiratory Medicine, Groote Schuur Hospital, Cape Town
[3] Radiation Oncology, Frere Hospital, East London
[4] Radiation Oncology, Provincial Hospital, Port Elizabeth, South Africa

A prospective randomised study was undertaken in patients with limited disease small cell carcinoma of the lung between March 1990 and August 1993. Doxorubicin, 50 mg/m^2, and vincristine, 2 mg iv on day 1 was given with either cyclophosphamide, 800 mg/m^2 (CAV) or etoposide, 60 mg/m^2 iv on day 1 and 120 mg/m^2 orally on day 2 to 5 (AVE). Responding patients were to receive 6 cycles of chemotherapy at 3-weekly intervals followed after 2 weeks by mediastinal irradiation.

	CAV	AVE	
Patients	38	43	
Complete response rate	32%	51%	($P = .07$)
Partial response rate	29%	23%	
Median survival	12 mo.	14.5 mo.	($P = .15$)
Leukopenia Grade 3	18%	7%	
Grade 4	11%	2%	($P = .03$)
Paraesthesiae	24%	23%	

No patients developed doxorubicin cardiomyopathy. This confirms the role of etoposide in first line chemotherapy for SCCL. Its use in combination with doxorubicin may be preferable to its use with cyclophosphamide in view of the low toxicity and efficacy observed.

86 POSTER

PRELIMINARY RESULTS OF A STAGE ORIENTATED MULTIMODALITY TREATMENT INCLUDING SURGERY FOR SELECTED SUBGROUPS OF LIMITED DISEASE SMALL CELL LUNG CANCER (SCLC)

W. Eberhardt, H. Wilke, G. Stamatis, S. Kolks, M. Stuschke, M.R. Müller, L. Schlenger, M.R. Nowrouslen, M. Stahl, U. Klaassen, A. Haarstrik, U. Fuths, D. Greschuhna, N. Konietzko, S. Seeber
Department Int. Med. (Cancer Res.), Essen University Medical School, Hufelandstaße 55, 45122 Essen, Germany

Since 6/91, 38 patients (pts) with limited disease SCLC (mediastinoscopy obligatory) have been entered into this ongoing trial. Pts with stage I and II were treated with 4 cycles cisplatin (50 mg/m^2 d 1 + 7) and etoposide (170 mg/m^2 d 3, 4, 5) = PE, q d 22 followed by restaging and surgery. IIIa pts were treated with 3 cycles of PE, q d 22 followed by one cycle simultaneous RTx/CTx (45 Gy, 1, 5 Gy twice daily within 3 weeks; P 50 mg/m d 2 + 9 of RTx, E 100 mg/m^2 d 4, 5, 6 of RTx) followed by remediastinoscopy and operation. IIIb pts were treated with 4 cycles PE, q d 22 followed by sequential RTx or 3 cycles PE plus 1 cycle of PE with simultaneous RTx (50 Gy, conventional fractionation, 2 Gy daily for 5 weeks). *Pts characteristics:* m/f 26/12; age 55 (34–69); PS 1 (0–1); Stage I 6, II2, IIIa 17, IIIb 13. *Results:* after CTx +/− RTx cCR 14; PR 21, CR/PR 35 (92%), MR 2. TOXICITY (WHO): lucopenia 3° 25%, 4° 10%; Infection 3 ° 10%, 4 ° 5%; thrombocytopenia 3°/4° 20%; diarrhea 3° 5%. One pt died of treatment related septicemia. Seventeen out of 25 (68% (stage I 6/6; stage II 2/2; stage IIIA 9/17)) pts underwent R0 resection including 7 (28%) pCR's. So far CNS relapses were the only site of failure in 7/17 pts who had R0 resection. None of them failed locoregionally. The median observation time for pts alive is 15 (3–46) months (mts). The median survival for all 38 pts is 29 (3+–46+) mts; stage I–IIIA not yet reached (3+–46+ mts), and R0 resection not yet reached (5+–46+ mts, 71% at 27 mts); stage IIIB 15 (6+–35+)mts. *Conclusions:* This intensive stage oriented multimodailty program is tolerable and highly effective for LD SCLC. Of note is the high local tumor control rate (100%) of pts with stage I–IIIA who underwent R0 resection.