adriamycin- ($P = 0.03$) had a positive impact on survival in both series of pts suggesting a potential benefit of a prolonged treatment when adjusting for the intensity of the first regimen.

92 POSTER

CPT 11 (IRINOTECAN) IN PRETREATED SMALL CELL LUNG CANCER (SCLC): A PHASE II STUDY IN PATIENTS PROGRESSING AFTER A FIRST RESPONSE (PRELIMINARY RESULTS)

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The standard combination chemotherapy of SCLC is an etoposide based regimen. After failure of this regimen the prognosis is very poor although the use of a rescue regimen still displays clinical activity.

It has been already suggested that investigational new drugs should to be assessed in second line therapy in SCLC and that a RR $\geqslant$ 10% among 29 patients would be relevant for the screening of active new compounds.

CPT11 is a new DNA topoisomerase I inhibitor active in colorectal cancer and other solid adult tumors.

22 patients with progressive extensive SCLC after a prior response on a VP16-based chemotherapy have been so far entered onto the study. Sex ratio M/F =19/3; median age = 57.2 (43–72). Performance Status 0 = 14%; 1 = 45%; 2 = 41%. Median number of involved organ 4 (1–6) with liver (27%), lung (22%), lymph nodes (16%) and brain (11% of patients).

57 cycles at the planned dose of 350 mg/m^2 every 3 weeks have been delivered with a median Relative Dose Intensity of 0.95 (0.78–1.03).

Efficacy: One CR and three PR have been observed among the 15 evaluable patients.

Safety: The incidence of grade 3 and 4 toxicity per cycle has been: neutropenia: 49% (with febrile neutropenia sepsis in 14%), delayed diarrhea: 18%, nausea vomiting: 14%.

Conclusion: The activity of CPT 11 in SCLC is likely to be attractive on the basis of these preliminary data. Neutropenia is clearly the dose limiting toxicity in this population of pretreated patients with frequent occult bone marrow involvement.

93 POSTER

A NEW STAGING SYSTEM FOR SMALL CELL LUNG CANCER (SCLC): A PROPOSAL

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The staging system should aim at four goals: (1) to define more accurate prognosis for individual pts; (2) to help in treatment planning in clinical practice; (3) to better compare therapeutic results in clinical trials; and (4) to define optimal risk groups for pt stratification in prospective studies.

From 2/85 to 6/93, 173 consecutive pts with SCLC received treatment tailored to disease extent. Fourteen out of 16 pts with stage I and II, 25/62 with stage IIIA and 5/37 with stage IIIB were subjected to surgery plus chemotherapy (CT) and RT (chest and brain). Pts with inoperable stage I–II (2/16) and III (IIIA 37/62, IIIB 32/37) received CT followed by RT while CT +/− symptomatic RT was administered in pts with stage IV disease. In all pts CT consisted of CAV-like regimens and/or cisplatin + VP16. The 5-year results (%) are as follows:

		Extent		Stage				
	Total	Limited	Extended	I	II	IIIA	IIIB	IV
FFP	16	24	0	54	50	22	15	0
Survival	16	26	0	67	65	19	27	0

Our data confirm the prognostic value of limited vs extended SCLC. However, analyzing our data according to a different stage grouping we obtained the following results:

New stage grouping	Stage (TNM)	% FFP (5-yrs)	% Survival (5-yrs)
Limited (L)	I–II–IIIA (T3N0)	48*	49**
Locally-extended (LE)	IIIA (T3N1–2)-IIIB	19*	22**
Extended (E)	IV	0*	0**

*L vs LE $P = 0.007$ *L vs E $P = 0.0001$ *LE vs E $P = 0.0001$ **L vs LE $P = 0.0025$ **L vs E $P = 0.0001$ **LE vs E $P = 0.0001$

This 3-stage grouping seems to better correlate with long-term results and may represent a more reliable staging model for SCLC.

94 PUBLICATION

SMALL CELL LUNG CANCER (SCLC) AND LONG-SURVIVORS. A REVIEW OF 276 PATIENTS (P)

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We reviewed 276 patients (pt) with histologically confirmed SCLC in a single institution from January 1981 to May 1992. They were treated with three different combination chemotherapy regimens. Among 251 evaluable patients only 18 (7.17%) were alive after two years (y). All these patients were men with a median age of 59 y. All but four had Limited Disease (LD). Four patients were treated with ECCP regimen (VP-16, CYC, CcNU, prednisolone), 4 with ECCA (VP-16, CYC, CcNU, ADM) and 10 with ECAP (VP-16, CYC, ADM, PCB). Among the 18 pt, 5 pt underwent chest radiotherapy and also 5 underwent prophylactic brain irradiation. Fifteen pt got a complete response (CR) and the time diagnosis-treatment was brief with a median time of 3.3 days. All the 18 pt had 0–1 ECOG performance status (PS) and most of them (15/18) a PS = 0. The 4 pt with Extensive Disease (ED) had disease in contralateral axila (1), bone and liver (1) and 2 pt were classified as ED because of exclusively having mediastinal syndrome. The median survival was 51 months (26–89 m) and, in May 1994, 9 pt were alive, 8 had died and 1 had disappeared on follow-up. Seven pt lived more than 5 y (2.78%). This results confirm that stage (LD), high PS and getting a CR are the main prognostic factors and, although relapses may exist after 2 y of survival, two-thirds of the patients being then free of disease will not relapse in the future. To find new drugs with more cytotoxic power is mandatory.

95 PUBLICATION

FOUR VERSUS 6 COURSES CISPLATIN ETOPOSIDE (E.P.) WITH EARLY CHEST RADIOTHERAPY. A RANDOMIZED STUDY IN SMALL CELL LUNG CANCER (SCLC)

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Despite several trials testing increased dose intensity, alternating drug administration etc. the survival of patients (pts) with SCLC has not improved. Early chest radiotherapy in pts with Limited Disease (LD) has been shown to improve patients' survival. In an effort to reduce toxicity we have compared the efficacy and toxicity of 4 courses (Group A) versus 6 courses (Group B) of EP chemotherapy combined with early chest radiotherapy. In a randomized study 52 evaluable pts have been treated with E.P. (Etoposide 120 mg/m^2 days 1–3, Cisplatin 80 mg/m^2 day I). All responders have been irradiated after the 4th course. Objective Response (O.R.) for Group A was 16/24 = 66%, with 5 CRS 20% and 11 PRS 46%, Group B OR: 21/28 = 75% with 7 CRS 25% and 14 PRS 50%. Median Time to progression group A: 8 mo group B: 13 mo ($P = 0.050$) Median Survival group A: 9 mo (5–28+) group B: 12.5 mo (6–43+) ($P = 0.033$). Median Survival LD pts group A: 15.6 mo, Group B: 20.5 mo (N.S.). Extensive Disease (E.D.) Group A: 7.5 mo, Group B: 11.5 mo ($P = 0.027$). Myelotoxicity and renal toxicity were not significantly different. We consider 4 courses inferior to 6 courses even with early radiotherapy. E.D. patients seem to benefit more from the two extra courses.

96 PUBLICATION

NONESOPHAGICAL EXTRAPULMONARY SMALL CELL CARCINOMA

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Extrapulmonary small cell carcinoma (ESCC) is a well known but uncommon neoplasm of uncertain origin. In spite of its rarity, the appearance of this type of tumor has been described in various organs of the economy. Of these, the esophagus has usually been reported as the most common location.

Eight patients with nonesophagical small cell carcinomas have been evaluated in our service between 1988–1995, constituting 2.2% of all small cell carcinoma (SCCs) that we have seen in the same lapse of time.

Histologically, seven cases were pure ESCCs and one was combined with adenocarcinoma. Immunohistochemical studies were performed in three cases, and in one of them, electron microscopy in addition. Only two patients were women. The ages of the eight patients ranged from 15–70, with a median of 62.5 years. Primary tumor locations were: colorectal (2), upper aerodigestive tract (2), urogenital (2: 1 prostatic), peritoneal (1), presenting one of the patients extensive abdominal disease of unknown primary origin. Five limited (LD) and three extensive diseases (ED) were found. In our series, initial treatments used, were chemotherapy (CHT) alone in five cases, surgery plus CHT in one, surgery plus radiotherapy (RT) in one, and surgery alone in one. The results were six complete remissions (CR) and two progressions (P). Overall survival median (from diagnosis), was 17 months (R: 1–68), being 20 months (R: 1–68) for patients with LD, against 16 months (R: 6–18) for the group with ED. There were two long term survivals (>2 years), which were treated with surgery plus RT and surgery plus CHT respectively.

Because of the low incidence of ESCC, and the responses and survivals observed by us and in other reports, it would be necessary the achievement of multicentric trials to standardize therapy.

97 PUBLICATION

CHEMOTHERAPY VERSUS CONCURRENT RADIO-CHEMOTHERAPY SCHEDULE IN SMALL CELL LUNG CANCER LIMITED DISEASE

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Out of 72 patients with small cell lung cancer (SCLC), limited disease 33 have been treated with chemotherapy only according to protocol 1 (HEMO) and 39 have been treated with concurrent radio-chemotherapy according to protocol 2 (KORHA). Analyzing according to the therapeutic protocols, the objective response has been achieved with 26 (79%) patients in HEMO group and 37 (95%) patients in KORHA therapeutic group. The objective response rate has been statistically significantly higher in KORHA group compared with HEMO group ($P < 0.05$). The individual statistical analysis of complete and partial remissions has shown statistical significantly higher rate of complete remissions in KORHA radiotherapeutic group ($P < 0.05$) compared with the HEMO group. The analysis of survival curves of the therapeutic groups has demonstrated that statistically significant difference is existing in survival among HEMO group on one side and KORHA group on the other side, ($P < 0.05$) in favour of radiotherapeutic group (median and two-years survival 10 months and 11%, versus 16 months and 32%). Therefore, the inclusion of thoracic irradiation in combined treatment of examined patients with SCLC having limited disease has resulted with statistically significant improvement of survival compared with patients treated with chemotherapy only.

98 PUBLICATION

PROSPECTIVE STUDY WITH CARBOPLATIN, VINCRISTINE, ETOPOSIDE I.V., AND ETOPOSIDE IN PROLONGED ORALLY DOSAGE, AS FIRST LINE CHEMOTHERAPY IN SMALL CELL LUNG CANCER

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The combination of etoposide and cisplatin now appears to have the best therapeutic index of any combined chemotherapeutic regimen used in small cell lung cancer (SCLC), and it allows the addition of some "thirds drugs" of probed efficacy, e.g. vincristine (V), without prohibitive hematologic toxicity. The use of carboplatin (C) instead of cisplatin is eventually preferable because it has fewer side effects with a similar efficacy. Etoposide (E) is the most active drug as single agent, and has been demonstrated the influence of dosage regimens in therapeutic results in SCLC. We report a prospective study with C, V, intravenous E, and E in prolonged orally dosage, as first line chemotherapy (CHT) in SCLC.

Seventy-seven patients (pt) with histologically confirmed diagnosis and a minimum performance status (PS) value (ECOG) of 2, were included from November 1991 to November 1994. Pretreatment evaluation consisted of complete medical history and physical examination, complete blood counts, liver and kidney function tests, chest roentgenograms, CT scans of chest and abdomen, bone marrow aspiration and biopsy, and fiberoptic bronchoscopy. The planned treatment consisted of C 350 mg/m^2 I.V. day 1, E 100 mg/m^2 day 1, V 1.4 mg/m^2 I.V. day 1, and E 50 mg/24 hr days 2–2, repeated every 28 days for six courses. Twelve pt were considered not evaluable. Six pt received less than two courses. Three pt were lost to follow-up. Two pt were wrongly included. One pt was wrongly diagnosed. Sixty five pt were evaluable, sixty three men and two women. The ages ranged from 38–75, with a media of 60.2 years (median: 62). Staging was performed according to VALg criteria: 40 (61.5%) cases of limited disease (LD) and 25 (38.5%) extensive disease (ED). We obtained an overall remissions rate of 78.5%, with 21 (32.3%) complete remissions (CR) and 30 (46.2%) partial remissions (PR). The median survival time was 300 days in patients with LD and 240 in those with ED, with an overall value of 251.5 days (R: 30–1020). Forty-five percent of the pt with LD got CR, and 27.5% PR. Twelve percent of pt with ED got CR, and 76% PR. There were five long-term survivals (>2 years). There was 1 toxicity secondary death (febril neutropenia). Observed grades 3 and 4 toxicities (WHO) were: anemia 21 pt (32.3%), leucopenia 10 pt (15.4%), thrombocytopenia 6 pt (9.2%), nausea-vomiting 2 pt (3.1%), alopecia 8 pt (12.3%), and neurological 1 pt (1.5%)

In conclusion, in our experience, this is an effective regimen in SCLC treatment, and also with an acceptable toxicity (especially alopecia and nausea-vomiting).

1063 POSTER

THE EFFECT OF CONTINUING SMOKING ON LATE RELAPSES AND SECOND PRIMARY CANCERS IN LONG-TERM SURVIVORS WITH SMALL-CELL LUNG CANCER (SCLS)

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From 1981 to 1992, 338 consecutive patients with untreated SCLC received standard therapy at our Institution. Of the 338 patients, 23 (6.8%) were alive and cancer-free two or more years from initiation of therapy. The other 315 patients died or relapsed with SCLC before two years. Follow-up time from initiation of therapy is 2.1 to 1.1 years (median 4.6) for the 23 patients. Six of the 23 patients (26%) developed recurrent SCLC 2.23 to 4.6 years (median 3.4) after beginning therapy. Four of the 23 patients (17%) developed one second primary cancer (SPC) 2.5 to 7.7 years (median 3.9) after initiating therapy. SPC diagnoses included: non-small cell lung cancer, gastric adenocarcinoma, squamous cell carcinoma of the floor of the mouth and carcinoma metastatic, to the neck of occult primary site. The cumulative actuarial risk of developing recurrent SCLC at five years is 39%. The cumulative actuarial risk of developing SPC at 5 and 8 years is 20% and 40% respectively.

Five patients continued to smoke after initiating therapy for SCLC, and 18 did not. Four of those who continued to smoke redeveloped cancer: recurrent SCLC (Three patients) and carcinoma of the floor of the mouth (one patient). As compared to patients who stopped smoking the Cox relative risk for developing recurrent SCLC or a SPC was 2.2 (95% CI, 0.6–8.4) in patients who continued to smoke (log rank test, $P = 0.22$). The corresponding relative risk for SCLC recurrence was 2.9 (95% CI, 0.6–14.5; log rank test, $P = 0.17$).

These data are suggestive of an increased risk of late relapses and SPC in 2-year cancer-free survivors with SCLC who continued to smoke after initiating therapy, although relative risks do not reach statistical significance. A study with larger number of cases is warranted.

1078 POSTER

RANDOMIZED COMPARISON OF ETOPOSIDE-CISPLATIN VS ETOPOSIDE-CARBOPLATIN AND IRRADIATION IN SMALL CELL LUNG CANCER (SCLC): EVALUATION OF LONG TERM SURVIVAL

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Between 2/88 and 5/91, 143 patients (pts) with SCLC (82 extensive and 61 limited disease) were randomized to receive Cisplatin and Etoposide (PE) or Carboplatin and Etoposide (CE). Responders, received concurrently with the 3rd cycle of chemotherapy chest irradiation, while CR's received additionally prophylactic cranial irradiation. No statistically significant difference was observed in the response and survival between