Results:

Stage	RR (%)	CR (%)	PR (%)	Median survival (months)
LS + ES	89	62	27	13 (95% CI: 10–16)
LS	100	89	11	20 (95% CI: 15–25)
ES	73	26	47	11 (95% CI: 9–13)

Main toxicity was hematological. Toxicity to VEC was mild but toxicity to PE was severe with grade 3–4 anemia in 66% of cycles, neutropenia in 48%, and throbocytopenia in 74%. There were two toxic deaths after PE. Six patients are alive and free of disease more than 24 months after treatment. Main cause of mortality was brain metastases (46%)

Conclusion: This high-density dose regimen is tolerable and very effective in limited stage patients. A significant number of pts in this stage become long survivors.

1040 POSTER*

Phase II study of paclitaxel as first line treatment for patients with extensive stage small cell lung cancer (SCLC)

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Paclitaxel has excellent antitumour activity in a variety of malignancies. Previous phase II studies in SCLC showed response rates of 34% and 41% but limited drug supplies restricted the number of cycles that could be given. We therefore performed a further phase II study in previously untreated patients with extensive stage SCLC. Paclitaxel 200 mg/m2 was given as a 3-hour iv infusion at 21 day intervals with dexamethasone, chlorpheniramine and cimetidine premedication. Thirty SCLC patients (19 male, 10 female, 1 not stated) of median age 66 years (range 34–76) were treated. At entry their median ECOG performance status was 1 (range 0–2). All patients had bidimensionally measurable disease, the commonest sites being (in order) lung, lymph nodes, liver, pleural effusion, bone and skin. The median number of treatment cycles administered was 2 (range 1–10). Among 27 patients analysed, 7 (26%) achieved a partial response and 4 (15%) stable disease. Six patients died on study, 13 stopped treatment with progressive disease and 5 with toxicity. The commonest toxicities were (in order) alopecia, peripheral neuropathy, nausea, aches/pains, fatigue. One patient experienced sepsis. We conclude that paclitaxel can be safely given to SCLC outpatients with a response rate of 26%. Further studies are required to evaluate its role in combination chemotherapy regimens for SCLC.

We thank Bristol-Myers-Squibb for supporting this study.

1041 POSTER

Pooled analysis of topotecan (T) in the second-line treatment of patients (pts) with sensitive small cell lung cancer (SCLC)

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Purpose: Topotecan is a new agent for the treatment of pts with sensitive SCLC. An analysis of pooled data was performed from 3 multicenter studies of pts with bidimensionally measurable SCLC who received T after progressing 3 months after one first-line regimen.

Methods: Topotecan was administered as a 30-min infusion at an initial dose of 1.5 mg/m^2 daily times 5 q 21 days until evidence of progression or unacceptable toxicity. Responses were confirmed by independent radiological review. Data presented are for the intent-to-treat population.

Results: A total of 726 courses (crs) were administered, median of 4/pt (range: 1–15 crs). A total of 168 pts (120 M, 48 F) were treated; mean age was 59 y (range: 31–76 y). Median performance status was 1 (range: 0–2). Response rate was 18% (95% CI 12.1–23.6%; 10 CR, 20 PR). Median time to response was 6 wks (range: 2–15 wks). Median duration of response (calculated from the time of documented response) was 23 wks (range: 8–51 wks). Median time to progression was 12 wks (range: 0.6–79 wks); 9 pts have not progressed. Median survival was 30 wks (range: 1.3–99 wks). One year survival was 21%; 20 pts remain alive. Grade 4 neutropenia occurred in 38% of crs and was associated with infection or ≥grade 2 fever in 4% of crs. Grade 4 thrombocytopenia and grade 3–4 anemia occurred in 11% of crs. Non-hematological toxicities were generally mild; alopecia, nausea, asthenia, and vomiting were reported most frequently.

Conclusion: Topotecan has activity with manageable toxicity in pts with sensitive SCLC. (Supported by SmithKline Beecham.)

1042 POSTER

A phase I study to investigate alternate sequencing of the combination gemcitabine followed by carboplatin in NSCLC

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Purpose/Methods: A phase I study evaluated the combination of gemcitabine and carboplatin in chemo-naive patients with NSCLC. Gemcitabine at a dose of 1000 mg/m^2 was administered on days 1, 8 and 15 of a 28 day cycle and carboplatin (dosing based on the Calvert formula) was given immediately prior to gemcitabine on day 1.

Results/Conclusions: Dose limiting myelotoxicity was seen at dose level 2, AUC of carboplatin 5.2 mg/ml/min. (n = 10). In order to determine if the toxicities of the combination were sequence related, 9 patients were recruited to the reverse sequence gemcitabine/carboplatin at an AUC of carboplatin of 5.2 mg/ml/min. on day 1.

Variable	Carbo/gem (10 pts)	Gem/carbo (9 pts)
Age range (median)	41–72 (64)	39–71 (58)
PS 1, 2	9, 1	9, 0
Adenocarcinoma	3	1
Squamous	4	1
Large cell	3	2
Unspecified	–	5
Stage IIIb, IV	3, 7	6, 3
Cycle range (median)	1–6 (3)	2–6 (4)
Grade III/IV Toxicities	% of cycles (n = 31)	% of cycles (n = 32)
Neutropenia	58.1	50.3
Thrombocytopenia	35.5	43.7

Evaluation of the toxicity and encouraging efficacy of this combination continues.

1043 POSTER

99m-Tc-sestamibi extrusion rate correlates with resistance to cytotoxic treatment and distant metastasis in non-small cell lung cancer

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Purpose: Application of a test that reliably evaluates multi-drug resistance is missing. Tc-99m radiolabeled hexakis-2-methoxy-isobutyl-isonitrile (99mTc-sestamibi) is recently shown to be extruded from cells through p-glycoprotein activity. In the present study we examined the up-take and extrusion rate of the radiotracer in 25 patients with advanced non-small cell lung cancer undergoing chest radiotherapy, using a novel scintigraphic technique based on simulation guided pin-hole imaging.

Methods: Using a Radiotherapy simulator a 4 cm of diameter area, was marked on skin of patients, above the tumor area. Each patient received 20 mCi (740 mBq) of 99mTc-sestamibi in the antecubital vein. 10 min after the injection, a gamma camera provided with a pinhole collimator able to scan an area of 12 cm in diameter was placed on the marked skin area. Standard five minute images were taken to collect 10^5 to 2×10^5 counts. The same procedure was repeated at 120 min. post-injection.

Results: 6/25 (24%) of tumors showed 1.3–1.7 times higher extrusion rate as compared to normal lung. Increased tumor clearance of the Tc-sestamibi significantly correlated with resistance to radiotherapy ($p = 0.05$) as well as the existence of distant metastasis ($p = 0.008$). Patients with known resistance to chemotherapy had higher extrusion rate as compared to chemotherapy naive patients ($p = 0.01$).

Conclusions: It is concluded that functional imaging of lung cancer with Tc-sestamibi may have a role in predicting response to cytotoxic treatment and in identifying tumors with aggressive behavior.