Results: The median number of cycles given was 3 to 4.

In both the day 1 & day 2 cisplatin studies, there was a high rate of omission (34% and 52%) of infusions of gemcitabine on day 15 because of thrombocytopenia. This was less than 20% in the day 15 cisplatin studies.

Conclusion: No conclusion can be made on relative survival and response rates as this depends on patient selection. The day 15 regimens are associated with the best tolerability.

Drug exposure duration is important to the activity of phase specific agents (eg gemcitabine).

1071 PUBLICATION

Conservative endbronchial treatment of non-small cell lung cancer

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Objectives were: to evaluate intratumoural injected bleomycine (BL) action during radiotherapy with dynamic fractions (RDF), second, to underline the effectiveness of photodynamic therapy (PDT) using heamatoporphyrin and metal vapour laser combining with conventional external beam radiation in patients (pts) with central type locally advanced NSCLC.

Methods: From 1989–1994 48 pts with NSCLC underwent intratumoural BL injections and RDF. The day we injected BL we use 4 Gy of RDF. Summary dosage of BL was 250.0–300.0 and 65 Gy of RDT. These pts were randomised with 46 pts of control group – only conventional RT.

From 1992–1995 16 pts with NSCLC underwent PDT with haematoporphyrin and metal vapour laser. 4 pts underwent this treatment with local reccurences after surgery. 8 pts with partial tumour response receive additionally – 40 Gy of conventional RT and were randomised with 12 pts control group – only RT.

Results: *First group of pts:* **1.** Partial tumour response we achieved in 31 pts (64.5%) with T2N2M0 and 12 pts (25%) with T3N2M0, no response in 5 pts (10.4%) with T3N3M0. **2.** Endobronchial BI injections causes coagulative tumour necrosis. *Second group of pts:* **1.** Full tumour response we advieved in 8 pts (50%), no response – in 4 pts (25%) with reccurens and 4 pts (12.5%) with T3N2M0 **2.** Combining PDT and RT improves rapidly pts PS and prolongs tumour relapse free period.

1072 PUBLICATION

Oral etoposide in patients with small cell lung cancer

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Purpose: To investigate the efficacy, tolerability, and survival of oral Etoposide (E) usage and prognostic factors influencing survival in small cell lung cancer (SCLC).

Methods: Between January 1993 to December 1996, histologically newly diagnosed and previously untreated 49 patients (pts) (45 men, 4 women) were included. Pts were with age ≥70 (23 pts) and pts who were unsuitable candidates for standard intravenous (IV) chemotherapy (CT) with age <70 (26 pts). Median age was 70 (43–81) and all pts had ECOG PS ≤ 3. Thirty pts (%61) had limited disease, while 19 pts (%39) had extended disease. It was given E capsules orally 50 mg bid for 10 days every 21 days as outpatiently. After 3 courses, responses were evaluated radiologically. In responded pts therapy continued until either progression or unexceptable toxicity occurred. Response and toxicity were evaluated according to WHO criterias.

Results: Eleven (%22) pts had partial responses, 17 (%35) pts had stable disease, and 21 (%43) pts progressed. No complete response was seen. In responded pts, response durations were between 17–154 weeks (median 36 wks). After observation of mean 23 wks (range 1–164 wks) only 4 pts (%8) are stil alive. Mean survival was 23 ± 1.4 wks (%95 CI 20.3–25.8) and were between 1–164 wks. One-year survival was %17 (SE:5). Totally, 207 courses (median 4, range 1–13) were given. Tolerance to oral E therapy was very good. No grade III/IV toxicity was seen. In univariate analyses by log rank test, ECOG PS (0–1 vs 2–3), weight loss (< vs ≥%5), stage (limited vs extended), erythrocyte sedimentation rate (ESR) (< vs ≥30 mm/h), serum albumin level (< vs ≥3.5 gr.dl), addition of radiotherapy (RT) (–/+) and response to CT (–/+) were statistically significant ($p < 0.05$) as prognostic factors effective over survival. On the other hand, age (< vs ≥70), body mass index (BMI) (weak vs normal), hemoglobin (< vs ≥12 g/dl), LDH (≤470 vs >470 IU/L), delay in CT (≤ vs >2 wks) were not statistically significant. In multivariate analysis, ECOG PS ($p = 0.0014$), ESR ($p = 0.0068$), RT (+) ($p = 0.0012$) and response to CT ($p = 0.0009$) were still statistically significant.

Conclusion: Due to its easy application, good tolerability and efficacy, oral E can be preferred in SCLC pts, especially to whom standard IV CT could not be given because of several causes.

1073 PUBLICATION

Symptom control and clinical benefit in advanced non-small cell lung cancer: Early report of a randomized study of gemcicitabine monotherapy versus cisplatinum-vindesine

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Chemotherapy in advanced NSCLC results in a small survival benefit. More important is its role in symptom control and quality-of-life improvement. In phase II trials, single agent gemcitabine (GEM) showed to be active in NSCLC, with a clinical benefit or symptomatic response rate (RR) higher than the objective RR.

We initiated a prospective randomized trial to compare the objective RR and clinical benefit of cisplatinum-vindesine chemotherapy (PV) versus GEM monotherapy. Clinical benefit is scored by a patient visual analogue symptoms score, the evolution of the Karnofsky performance status (PS) and weight.

At the time of writing, 46 patients were randomized. Seventeen evaluable treatments were panel reviewed. For PV, we found 1 partial response (PR), 5 stable disease (SD) and 2 progressive disease (PD). For GEM this was 1 PR, 3 SD and 5 PD. Toxicity was analyzed in 53 cycles. The number of cycles with WHO grade III/IV toxicity in the PV arm was leukopenia 5, granulopenia 4, vomiting 2 and hair loss 3. For GEM, this was leukopenia 1 and diarrhoea 1 cycle. Clinical benefit was present in 2 PV patients (1 with objective PR, 1 with SD) and 3 GEM patients (1 with objective PR, 2 with SD).

Patients without objective response can nonetheless have clinical benefit from their chemotherapy. It is too early to draw further conclusions, but a trend towards lower objective RR and milder toxicity in the GEM arm is suggested. Updated results on a larger number of patients will be reported.

1074 PUBLICATION

Radiation related toxicity in patients with limited stage small cell lung cancer (SCLC) receiving irradiation on primary tumor site after intensive chemotherapy

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Purpose: In our past study 222 pts with limited SCLC received chest irradiation after standard chemotherapy. Acute radiation toxicity was 37.8%, pulmonary toxicity 80% and pulmonary fibrosis 83% at X-ray. In this study we evaluated the radiation related toxicity after intensive chemotherapy.

Methods: Fifty-three pts received local regional irradiation with doses 40–50 Gy after 2–3 courses of intensive chemotherapy with haematological support (ABMT – 14 pts, GM-CSF – 25 pts, polidan – 14 pts).

Results: Acute radiation related mucosal toxicity (oesophagitis, laryngopharyngitis) was seen in 59% of pts and pulmonary toxicity in 85% of cases at the period of time up to 3 months. The delayed local pulmonary fibrosis in the irradiation site was seen at X-ray in 85% of pts, whereas only 8% of them had clinical symptoms.

Conclusion: Pulmonary fibrosis did not worsened quality of life of pts with SCLC which was influenced mainly by the presence of residual tumor or local recurrence after CR and also by the presence of distant mts and is the same as in pts with standard chemotherapy. In pts with intensive chemotherapy was more acute radiation toxicity (59% vs 37.8%).

1075 PUBLICATION

Pair: Palliative accelerated irradiation regimen for non-small-cell lung cancer: Final results of the pilot study

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Purpose: In order to avoid overtreatment for patients with advanced non-small cell lung cancer (NSCLC) we have developed a palliative accelerated irradiation regimen (PAIR). Before the onset of a randomized trial in February 1994, we performed a one year pilot study testing the feasibility

of the regimen in comparison to the standard 60 Gy prescription. After first results had been published in 1996, a final evaluation was now made.

Methods: 34 patients with locally inoperable NSCLC UICC stage III (74%) and IV (26%) were treated with a total reference dose of 32 Gy to tumor and mediastinum in two daily single doses of 2 Gy (PAIR). They were compared to 183 conventionally irradiated historical controls (C) selected from a preexisting database according to study inclusion criteria (65% III, 35% IV). 105 of them had been irradiated with a total reference dose of 60 Gy (C 60).

Results: While, certain prognostic factors were rather unfavourable for PAIR patients, their overall survival was significantly better compared to C ($p = 0.006$; median survival 8.6 vs. 5.6 months). Compared to C 60, no significant difference in overall survival was found (median survival 8.6 vs. 7.5 months). This was also true for the comparison among stage III ($p = 0.06$) or stage IV patients only. Cox regression analysis showed Karnofsky performance index and N stage being independent factors (including also UICC-stage, local control, T-stage, weight-loss, treatment, and LDH).

Conclusion: In the final evaluation of the pilot study, the survival of the PAIR patients was well comparable to that of the control group, and was especially not worse than that of C 60. We consider the PAIR-regimen a short, cheap and feasible alternative to the standard prescription of 60 Gy in advanced NSCLC.

1076 PUBLICATION

Phase II trial of docetaxel and carboplatin in the treatment of advanced non-small cell lung cancer

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Purpose: Based on superior single agent docetaxel response rates in previously untreated (27% ORR) and pre-treated (21% ORR) patients (pts.) we initiated a phase II trial of docetaxel- and carboplatin-polychemotherapy in patients with stage III b-IV inoperable NSCLC.

Patients and Methods: Pts. with measurable disease without prior radio or chemotherapy, good performance status (PS) and without brain metastases. Treatment schedule consisted of docetaxel 90 mg/m^2 followed by carboplatin according to AUC 5, treatment was repeated at 3 week intervals for six cycles.

Results: 27 pts. have been included, 3 female, 24 male, mean age 60.4 (range 44–71) PS 0/1/2 in 6/14/7 pts., histology: squamous cell carcinoma: 13, adenocarcinoma 3, anaplastic cell carcinoma 8, large cell carcinoma 3; stage III B 16, stage IV 11.25 pts. were evaluable according to response (two pts. had allergic reactions), CR 0 and PR 9 (36%) were observed lasting 17 to 29 +weeks. Grade 3 or 4 granulocytopenia occurred in 55.5% of the pts.. Non haematological toxicity (Grade 1–2), e.g. nail alterations and oedema, occurred in 66.6%.

Conclusions: Based on this preliminary analysis we conclude that the combination of docetaxel/carboplatin is active and well tolerated for the treatment of NSCLC.

1077 PUBLICATION

Symptom distress in patients with advanced non-small cell lung cancer treated with chemotherapy

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Quality of life (QoL) assessment became one of the most important endpoints of clinical studies in advanced lung cancer, disease with high expression of symptom distress. In a prospective, phase III study, 210 patients were randomized to receive MVP (cisplatin 120 mg/m^2) or MVC (carboplatin 500 mg/m^2) chemotherapy regimen for IIIb or IV stage of squamous cell lung cancer. Differences between cisplatin and carboplatin group were not observed by assessment of tumor response (RR = 34% for both groups) and functional status by ECOG scale. For assessment of QoL we used Rotterdam Symptom Checklist (8 items specific for lung cancer and 3 items related to social dimension of life were added) on 44 patients. Compliance in filling questionnaire was 100%. The leading symptoms and aspects of life quality during chemotherapy were evaluated.

At presentation, the commonest five items were: worrying, cough, tiredness, shortness of breath and nervousness. Analyzing all the cycles applied (177), the leading five items were: shortness of breath, financial troubles, worrying, cough and tiredness. In cisplatin and carboplatin group there were no changes during treatment (Wilcoxon), except worsening of financial troubles after first cycle of chemotherapy, in cisplatin group. Comparing two groups, cough was less expressed in carboplatin group, but only after third cycle of chemotherapy (Mann-Whitney).

In conclusion, the commonest symptoms in patients with advanced lung cancer cover different domains -physical, psychological and social, including general as well as lung cancer specific problems. All of them could be emphasized thanks to multidimensionality of Rotterdam Symptom Checklist. We could also see that all symptoms persisted during treatment – it appears that in spite of 1/3 of responding patients, chemotherapy could not help in alleviation of symptom distress, in advanced lung cancer.

1078 PUBLICATION

Steroid hormone receptors in lung cancer: Differential expression, function and clinical significance

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Epidemiolgic data suggest a clinical role of steroid hormones in lung cancer: women with lung cancer have a significant longer survival than men, on the other hand use of exogeneous estrogen seems to increase the risk of lung cancer.

By means of PCR technique, ligand binding studies and immunocytochemistry we studied 15 SCLC lines and 17 NSCLC lines for the expression of steroid hormone receptors: The glucocorticoid receptor (GR) and the vitamin D receptor (VDR) are ubiquitously expressed. Among the sex steroid receptors estrogen receptors (ER) are expressed in 30% of NSCLC lines but not in SCLC lines, progesterone receptors (PR) are present in 75% of NSCLC lines but rarely in SCLC lines, androgen receptors can be found in 50% of NSCLC lines but rarely in SCLC lines. Receptor expression in 51 primary tumor samples from NSCLC confirm the high expression rate of GR and VDR. Among different histologies adenocarcinomas show the highest rate of sex steroid receptor expression. Proliferation assays in six lung cancer cell lines reveal no significant effect in SCLC lines. In NSCLC lines glucocorticoids inhibit growth, vitamin D and progesterone have no effect whereas estrogen stimulates growth in a cell line stemming from an adenocarcinoma (NCI-H23).

Data suggest that glucocorticoids may be incorporated in NSCLC therapy. Estrogen may have a proliferative effect on adenocarcinoma of the lung. However, survival advantage of female patients with lung cancer is not explained by differential steroid receptor expression.

1079 PUBLICATION

Role of 99mTc-Sestamibi for diagnosis, staging and follow up of patient with lung cancer

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Purpose: The aim of this work was to evaluate the clinical application of 99mTc-Sestamibi for diagnosis, staging and follow up of patients (pts) with lung cancer (LC).

Methods: Planar and SPET images were performed 30 and 90 min. after i.v. injection of 99mTc-Sestamibi in 19 pts (5 F; 14 M) with histologically proven LC (13 SCLC; 6 NSCLC) undergoing combined chemotherapy. In order to quantify Sestamibi uptake a Tumor/Background ratio (T/B) was calculated. 10 pts were also investigated after one and three months after chemotherapy.

Results: The mean T/B ratio in the studied pts was 1.50 (range 1.38–1.60), $p < 0.001$, before treatment. Out of 19 pts, 8 pts showed complete or partial response to the combined chemotherapy and parallel reduction of the mean T/B ratio – 1.26 (range 1.17–1.32), $p < 0.001$. Bone and brain metastases were visualized in 4 pts. In 7 pts it was established stable disease.

Conclusion: Our preliminary results show that 99mTc-Sestamibi is a useful, diagnosic method for pts with LC. Semiquantitative assessment of 99mTc-Sestamibi in LC was related to the tumor response after chemotherapy and may be used for evaluation and follow up of these pts.