## Lun 10

NON SMALL CELL LUNG CANCER :FEASIBILITY OF CONCOMITANT IRRADIATION AND CHEMOTHERAPY.

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Patients (pts) with non small cell lung cancer (NSCLC) with local extension and/or mediastinal involvement (stage III,UICC) still carry a particular poor prognosis. Short median survival time (MST) is a strong argument to add chemotherapy (CT) to radiotherapy (RT) with the intention of an acceptable total treatment time. We performed three feasibility studies with RT and concomitant CT and chose cis-Platinum (cP) or vindesine (V) as single agents and in a third study RT + cP + V. 16 previously untreated pts with NSCLC entered a study with simultaneous RT with cP. RT consisted in a median dose of 45 Gy; cP was administered in all pts as 120 hrs infusion ( 20 mg/qm/24 hrs ) during week 1,4 and 7. Continuous infusion has been reported to be less toxic and at least as effective as cP given by bolus. CR was observed in 3, and PR in 8 pts. Considering only stage III pts (n=10) MST is 11 months. From this study we concluded: concomitant RT with cP is feasible without major radiation toxicities ; an increase of RT dose appears possible. Since 1/85 we started a protocol with 55-60 Gy RT and cP (20mg/qm/24hrs for 100 hrs) during week 1,4 and 7 and weekly bolus of 3mg/qm V during week 2,3,5,6 and 8. In a third study, pts > 65 years were treated with V as a weekly bolus during 6 weeks without cP. Unpublished data of an ongoing randomized trial of the Southeastern Cancer Study Group suggests a better local response. Preliminary results with our two protocols, RT + cP + V (10 pts) and RT + V (10 pts) are promising without major toxicities.

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## Lun 11

CHEMOTHERAPY OF ADVANCED NON-SMALL-CELL LUNG CANCER WITH DDP AND HIGH-DOSE ETOPOSIDE

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Introduction: Cis-Platinum and VP-16 are active agents in the treatment of NSCLC with synergism in experimental models. A dose-finding study of VP-16 with a fixed dose of DDP led us to conclude that the maximally tolerated dose i.v. of VP-16 was in the range of 500 mg/m$^2$ per course. To define the activity and toxicity we started a phase-II-trial.

Patients and methods: Since 8/1983 41 patients with untreated inoperable NSCLC were entered into the protocoll until 3/84. 40 patients were evaluable for response and median survival time. Patients characteristics: 75 % ED. Median age 57 years. Performance-Status more than 70 % in all patients. Histology: 23 squamous cell, 9 large cell, 9 adeno carcinomas.

Dose schedule: DDP 100 mg/m$^2$ day 1
VP-16 170 mg/m$^2$ day 3/4/5

Results: The response rate was 16/40 patients (40 %). 2 patients (5 %) achieved a complete remission, 14 patients (35 %) a partial remission. The median survival time in responders is 13 months (follow up 16 months) including 3 early drug related deaths, in non-responders 8 months. The toxicity of the chemotherapy was a serious problem, 4 patients achieved a severe agranulocytosis, which leads to 3 drug related early death with septic fever.

Conclusion: The combination DDP and high-dose VP-16 did not improve the results of response and median survival time in NSCLC in retrospective comparison to regime with lower dosages of these drugs (own results). The side effects however are much more serious, especially the hematological toxicity. Therefore these dosages can't be recommanded in the treatment of patients with inoperable NSCLC.

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## Lun 12

HYPERFRACTIONATED RADIOTHERAPY OF BRONCHOGENIC CARCINOMA

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We have irradiated 1oo patients with small cell (SCLC) and non small cell lung cancer (NSCLC). 41 patients were treated twice daily and 59 with a conventional fractionation scheme. Patients with SCLC were irradiated either with 52 Gy/4o fractions/4 weeks in a hyperfractionated way or with 46 Gy/23 fractions/4.3 weeks. Patients with NSCLC received either 65 Gy/5o fractions/5 weeks (hyperfractionated schedule) or 6o Gy/3o fractions/6 weeks (conventional regimen). Concerning age distribution, tumor stage, Karnofsky index and previous treatment the respective groups were well balanced. In the case of patient with NSCLC life table (Kaplan-Meier estimate) showed no difference between the therapy schedules. Median survival was approx. 33o d. The treatment groups were not different with respect to progression-free interval and occurence of distant metastases. Concerning SCLC the Kaplan-Meier estimate of survival showed no significant difference between both groups, but in the hyperfractionated arm the results seem to be somewhat better. Median survival was 33o d after conventional treatment and exceeded 45o d after hyperfractionation. We found no difference concerning the occurence of distant metastases. Radiation pneumonitis occured in all groups but significant differences could not be seen. We therefore believe that we have no underdosage with the hyperfractionated regimens and that these schemes could be of some value treating rapidly proliferating tumors.

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## Lun 13

THE NEW ANTHRACYCLINE THP-ADM (4' -O-TETRAHYDROPYRANYL-ADRIAMYCIN) IN THE TREATMENT OF MALIGNANT PLEURAMESOTHELIOMAS

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Introduction: In the treatment of pleuramesotheliomas some drugs seem to be active. Doxorubicin as single agent is the most active drug reaching a response rate of approximately 40 % (Vogelzang 1984). The efficacy of the new anthracycline-analogue THP-ADM is similar or better to Adriamycin but the side effects are less pronounced. To assess the effectiveness and side effects we started a phase-II-trial.

Patients and Methods: Since 10/1983 13 patients with histologically proven pleuramesotheliomas were entered into the protocoll. 7 male/6 female with a median age of 57 years. The performance status of all patients was more than 70 %.

Dose schedule (Majima): 40 - 50 mg/m$^2$ i.v. bolus every 3 weeks.

Results: The response rate was 1/13 (7,6 %)partial remission.
7/13 (53,8 %) patients showed stable disease.
5/18 (38,4 %) had progressive disease.
The median survival time with a minimum observation period of 7 month was 9,5 month. In general, the side effects were extremely mild; we didn't see any severe cardiotoxicity. Gastrointestinal side effects are very rare.
In summary, the antitumor effect of THP-ADM as single agent in pleuramesotheliomas is only low. But the maximally tolerated dose appears to be much higher than 40 - 50 mg/m$^2$ per course. In the following trial we were going to use 70 - 75 mg/m$^2$ per course with still acceptable toxicity in the first 3 patients.

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