918

INTRAOPERATIVE RADIATION THERAPY (IORT): CLININCAL EXPERIENCES IN NON-SMALL-CELL LUNG CANCER. (NSCLC)

Geyer E., Smolle-Juettner F., Stücklschweiger G., Ratzenhofer B., Poschauko J., Kapp K.S., Leitner H., Pinter H., Friehs G., Hackl A.
University Clinic of Radiology, Dept. of Radiotherapy, Auenbruggerplatz 9, A-8036 Graz, Austria.

Locally advanced lung cancer represents a common disease in daily medical activity, and its poor prognosis is well known. Intraoperative radiation therapy has demonstrated to be a feasible approach for tumors, in which, due to their topographical location, doses necessary for local control cannot be delivered safely by external treatment (EBRT) alone. In addition, IORT has been demonstrated to be an attractive boosting modality in conjunction with surgery and/or conventional external beam radiation for a variety of tumors.
In a pilot study in 31 patients (age: 66.2y; range: 51-80; 20 squamous, 11 adeno- or large-cell T1:7, T2:16, T3:8, 11 nodal positive, all M0) we investigated the effect of IORT (10-20 Gy/electron beam 7-20 MeV) combined with EBRT (4 weeks after IORT 46-56 Gy, 2 Gy/day, 5 times a week delivered to both primary and mediastinum).
23 patients are avaluable. 13 had complete (CR), 8 partial (PR;50 to 97% regression) and 2 minor responses (MR). 6 patients relapsed. 12 patients died of the underlying functional impairments (6-45 ms after IORT). 7 died of tumor.The overall 5 year survival rate is 14.7% (comprising the incidental deaths), the recurrence-free survival rate is 53.2%.

919

SPLIT COURSE LOCAL IRRADIATION ALTERNATED WITH PLATINUM-CONTAINING CHEMOTHERAPY IN INOPERABLE STAGE III NSCLC.

G.Comella, G.F.Scoppa, G.Catalano, L.Brancaccio, A.Daponte, R.Casaretti, E.Micillo, A.Maiorino, C.Curcio, F.Vigorito, P.Comella. Oncological Cooperative Group, National Tumor Institute, Naples, Italy.

From January 1990 to February 1993, 54 consecutive patients affected by NSCLC with locally advanced disease were treated with combination chemotherapy (CH) including a platinum compound (CDDP 60 mg/sqm or CBDCA 300 mg/sqm i.v. d 1), epirubicin (50 mg/sqm i.v. d 1) and etoposide (100 mg/sqm i.v. d 1-3) every four weeks. Each cycle was alternated with local irradiation (RT)(300 cGy/d x 5 days), so that the whole program of treatment included 4 courses of CH and 3 phases of RT (total dose=45 Gy) in 13 weeks. Up to February 1993, 41 pts (squamous cell=23, adenoca=14, large cell=4; IIIA=27,IIIB=14) are evaluable for response and toxicity. Eight pts achieved a CR and 17 a PR, whereas 5 pts were in SD and 15 pts showed a PD during therapy. Therefore, 21 pts (51%) were judged to have obtained a major response (IIIA=15/27, IIIB=6/14), without a significant difference between pts treated with CDDP (12/21) and CBDCA (9/20). Median duration of responses was 33 (CDDP=39 vs CBDCA=29) weeks. Overall median survival of treated pts was 35 weeks (14 weeks for 20 non responder pts, 51 weeks for 21 responder pts). No significant survival difference was observed between CDDP- and CBDCA-Arm (38 vs 31 wks). The nadir of blood cell count was registered after 2 weeks from the start of each cycle, when a WHO grade 3-4 leukopenia was detected in 95% of courses (CDDP=100%, CBDCA=90%); while a WHO grade 2-3 thrombocytopenia was assessed only in 50% of courses. Only in three cases the bone marrow recovery was incomplete after 4 weeks. Anyway, CH was always administered at full doses. Nausea and vomiting were the most bothersome side effects, observed in all pts, but they were less severe in CBDCA-treated pts. Diarrhoea (35%), infections (26%) and arrhythmias (21%) occured with similar incidence in both groups. In conclusion, our experience confirmed the feasibility and the effectiveness of a combined modality treatment in NSCLC. CBDCA-containing treatment appeared somewhat less toxic but showed comparable activity to the CDDP-including therapy.

920

NON-RESECTABLE STAGE IIIA-B LUNG CARCINOMA: A PHASE II STUDY ON CONTINUOUS INFUSION OF CISPLATIN AND CONCURRENT RADIOTHERAPY (PLUS ADJUVANT SURGERY).

Ravasi G. Bedini AV, Tavecchio L, Milani F, Gramaglia A, Villa S, Palazzi M. Istituto Nazionale Tumori, Via G. Venezian 1, 20133 Milano. Italy.

Thirty-eight patients with non-resectable non-small-cell stage IIIa-b lung cancer were treated in a phase II study with radiotherapy (50 Gy in a 25-fraction split-course) plus concurrent continuous infusion of cisplatin given at a daily dose of 6 mg/m2. Adjuvant surgery was undertaken when feasible. Toxicity was mild to moderate. The probability of a partial or complete locoregional response at 4 weeks after treatment completion was 83%. Eighteen patients were resected. Overall 1-, 2-, and 3-year progression-free survival probabilities were 42%, 24%, and 21%. These figures were 63%, 37%, and 24% in observed survival curves. Patients with squamous-cell tumors had observed survival rates of 82%, 50%, and 28% at 1, 2, 3 years, compared to 42%, 19%, and 19% in patients with non-squamous histology. The high response and survival rates obtained at a low price according to toxicity require further investigation.

921

DNA CONTENT, DISTRIBUTION OF CELL CYCLE PHASES AND EGFR IN RESECTED NON-SMALL CELL LUNG CANCER. ITS PROGNOSTIC SIGNIFICANCE.

*Alberola V, *Marugán M, **Padilla J, **Bolufer P, **Blasco E, *Benet I *Llombart A, *García-Conde J.
*Division of Hematology and Medical Oncology. University Hospital. Valencia. ** Division of Byochemistry and Thoracic Surgery. Hospital La Fe. Valencia. Spain.

The aim of the study was to investigate the prognostic significance of flow cytometric determination of DNA ploidy plus S-Phase and expression of EGFR in resected non-small cell lung cancer. During 1989-1992 one hundred sixty patients were entered in a prospective assay. We analize 90 patients entered 1989-90;of which, 30 and 60 were adeno and epidermoid tumors respectively; stage I+II:60%, stage III: 40%. Median follow-up, 36 months. Fifty-eight (65%) patients had DNA aneuploid patterns; S-phase higher than 10% in 42 (51%); median EGFR was 65 pg/mg TP. At 36 months, 65% and 43% of stage I+II and III and 76% vs 40% of N0 and N+ patients were alive, respectively. There is no differences between diploid and aneuploid tumors. Low fraction S-phase was predictor of better survival only in subset of N0 lung cancer patients. Levels of EGFR higher than 65 pg/mg TP were not related with relapse. Study continue to analize patients from years 91-92. We concluded that prognostic significance of biologic factors need to be studied in a large prospective assay with prolonged follow-up.

922

RADIOSENSITIZATION FOR LUNG CANCER

V. Zharkov, Yu. Demidchik, A. Furmanchik, P. Moiseev, V. Kurchin, E. Schroeder, M. Hentschel. Cancer Research Institute, Minsk 22052, Belarus and Max Delbruk Center for Molecular, Berlin 0-1115, Germany.

Since 1983 till now 849 operable non small cell lung cancer patients were included in phase 2-3 studies of hyperglicemia, metronidazole, izometronidazole, cisplatin and AK2123.
Radiosensitizers were carried out at the time of the preoperative large fraction radiotherapy (TDF = 50). According to received data radiosensitization allows to increase significantly the tumor alteration and survival rates. Except metronidazole all approaches are well tolerated. Survival depends on stage, tumor differentiation, type of its growth, size and provided radiosensitization approach. The better results were achieved in cases of hyperglicemia and izometronidazole.

923

NEUROPATHY DURING TREATMENT WITH VINDESINE AND CARBOPLATIN IN PATIENTS WITH ADENOCARCINOMA OF THE LUNG.

Borg J, Borg K, Hansson S*, Agrenius V**, Lewensohn R***. Dpts of Neurology, Pulmonary Med.** and Oncology***, Karolinska Hosp. and Neurophys.* Söder Hosp., Stockholm, Sweden.

Peripheral nerve function was examined in twelve patients during treatment with Vindesine och Carboplatin due to inoperable adenocarcinoma of the lung. Paresthesias were reported by 6 patients. Reduced tendon reflexes were observed in 3 patients. The sensory nerve action potential (SNAP) decreased in all subjects when accumulated doses of Vindesine ranged 15-43 mg and Carboplatin 440-1700 mg. At higher accumulated doses the SNAP was unchanged or even improved. Nerve conduction velocity did not change. Vibratory thresholds increased mainly in parallell with SNAP decrease. Thermal and thermal pain thresholds did not change. Electromyography showed increased incidence of polyphasic single motor unit potentials at the higher accumulated doses. The data suggest an axonal neuropathy affecting large myelinated fibres and was subclinical in half of the patients. Key-words: Vindesine, Carboplatin, Neuropathy.