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Post-induction FDG-PET in NSCLC IIIA and IIIB: Correlation with morphometric tumor response after docetaxel (D)/carboplatin (C) chemotherapy in combination with erythropoietin

F. Griesinger[1], J. Leugering[1], F. Lahmann[1], C.P. Criée[2], H. Dalichau[3], B. Herse[4], J. Schirren[5], B. Hemmerlein[6], H. Leupold[1], R.-P. Baum[7]. *[1] Dept. Hematology and Oncology; [3] Dept. Thoracic Surgery; [6] Dept. Pathology, University of Goettingen; [2] Dept. Pneumology Lung Clinic Lenglern; [4] Dept. Thoracic Surgery Hospital Erfurt; [5] Dept. Thoracic Surgery Hospital Wiesbaden; [7] Dept. Nuclear Medicine, Bad Berka, Germany*

Objective: D/C combination chemotherapy (CTx) has shown high response rates in advanced NSCLC. Histologic tumor response after CTx as well as combined induction regimens are highly associated with systemic tumor control and potentially with cure. Metabolic tumor response by FDG-PET after induction CTx has been shown to be predictive of outcome in NSCLC. Finally, erythropoietin (EPO) may prevent the decrease of Hb-values (median of −2.7 g% in a previous study) and thus may increase efficacy of induction CTx. Therefore, the aim of the study was to correlate FDG-PET after D/C-EPO CTx with morphometry.

Patients and Methods: 38 NSCLC stage IIIA and IIIB pts were enrolled and received D 100 mg/m2 d1 and C AUC 7.5 d2 q21 days for 4 cycles. Epo was administered at a dose of 3 × 10,000 IU/week s.c. All pts. received adjuvant radiotherapy.

Results: Of the 38 enrolled patients, 28 are evaluable for response by CT-scan. 20/28 pts. (71%) achieved PR. 4 had SD and 4 PD (14%). 24 of 28 responders are evaluable for control-FDG-PET. 21/24 pts. (87%) had a decrease of SUV by >50%, 8/24 had a SUV < 2.5 (CR). Six of these 8 pts. have been resected and specimens were morphometrically analyzed. In all 6 cases, no vital tumor cells (regression grade III = morphometric CR, according to Thomas et al., JCO 2000) were identified in the specimens. In contrast to the previous study performed without EPO, Hb-levels increased by a median of 0.3 g%.

Conclusion: Morphometric regression grade III after induction CTx correlates highly with metabolic CR by FDG-PET. After a median follow-up of 21 months, all patients with CR by FDG-PET survived disease free. Thus FDG-PET may represent a non-invasive diagnostic tool to predict pathologic response and potentially long term outcome in stage III NSCLC.

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Continous accelerated hyperfractionated radiotherapy (CHART) plus chemotherapy (CT) with vinorelbine (VB) and cisplatinum (CDDP) in locally advanced NSCLC (TOG-011 study)

F. Oner Dincbas[1], S. Koca[1], A. Altinel[1], T. Hancilar[2], M. Cavusoglu[2], S. Turhal[3], N. Uskent[4], M. Ozguroglu[5], S. Okkan[1]. *[1] Cerrahpasa Medical School, Radiation Oncology, Istanbul, Turkey; [2] Okmeydani Hospital, Radiation Oncology, Istanbul, Turkey; [3] Marmara Medical School, Medical Oncology, Istanbul, Turkey; [4] Gulhane Military School, Medical Oncology, Istanbul, Turkey; [5] Cerrahpasa Medical School, Medical Oncology, Istanbul, Turkey*

Purpose: A phase II study was conducted to evaluate the efficacy and tolerability of CHART plus daily CDDP plus sequential CT with VB and CDDP.

Materials and methods: Patients histologically proven with NSCLC, stage III, less than 70 years old, whose performance status was 0-2 and who had no prior therapy were included. Twenty-two patients enrolled to the study. Their median age was 52 years old (31-70 years). Stage was 3B in 16 and 3A in 6 patients. Two cycles of VB 30 mg/m2 and CDDP 75 mg/m2 were given in 3 weeks apart. Then, patients were treated by CHART with CDDP as a radiosensitizer 6 mg/m2 (max. 10 mg) daily. 54 Gy in 36 fractions were given 3 times a day over 12 consecutive days. The dose per fraction was 1.5 Gy. Two cycles of CT were applied three weeks after CHART with the same schedule.

Results: All of the patients completed the therapy. At the end of the therapy there were 4 CR, 12 PR and 6 stationary diseases. Fifteen of the patients died and 7 patients were alive during evaluation. 3 of them were with disease (19, 25, 40 months) and 4 were without disease (15,10, 4, 4 months). Median local control duration was 10 months (6-22) and median survival time was 12 months (4-14) and 1-year survival rate was 47,6%. Median disease-free survival was 7 months (4-22). Distant metastases were found in 9 patients. Grade 1-2 toxicity in 18 patients and grade 3 toxicity in 6 patients were observed. Esophagitis was the most common side effect. Grade 1-2 dysphagia were seen in 13 patients and grade 3 dysphagia was observed only in 2 patients. Four patients developed grade 3 nausea and vomiting during CT. There was no serious hematologic toxicity due to CT. CDDP dose was reduced in two patients due to grade I nephrotoxicity. Five patients developed radiation pneumonitis and 7 had radiation fibrosis. They all recovered by medical therapy.

Conclusion: This combined modality regimen appears to improve the response rates and local control and median survival with mild toxicity.

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Final results of a phase II study of Gemcitabine (G) and Platin (P) in advanced non-small cell lung cancer (NSCLC): Long-term follow up and intention-to-treat analysis

C. Sacco[1], G. Cartei[2], A. Sibau[1], A. Bearz[2], M. Gusella[3], A. Iop[4], E. Vigevani[5], V.M. De Pangher[6], A. Lucenti[7], G. Tabaro[2], R. Talamini[8]. *Oncology Divisions: [1] Udine; [2] CRO-Aviano (PN); [3] Rovigo; [4] Latisana (UD); [5] Tolmezzo (UD); [6] Monfalcone (GO); [7] Trento; [8] Statist and Epidemiol, CRO-Aviano (PN), Italy*

Introduction: G, a nucleoside analogue, has efficacy in BSCLC, with synergism or additive effect both *in vivo* and *in vitro* with P. We report final results of a prospective multicentric phase II study on the safety profile, clinical efficacy and survival obtained with our regimen G 1500 mg/m^2, administered as a 30' i.v. infusion on day 1 and 8, and P 100 mg/m^2 on day 8, given on 21-day cycle (c) (Ann Oncol 10 (5): 57–62, 1999). This regimen is different from Others's because of P was delayed to the 8th day and only 2 accesses/c.

Results: From Oct '96 to Feb '98, one-hundred-five consecutive untreated pts (90 M), cytological or hystological NSCLC proved, entered the study; median age 61 y.rs (34–78 y.rs); P.S. ECOG 0 in 57 pts, 1 in 41, 2 in 7; adenocarc. 39 pts, squamous cell 43, large cell 3, undiffer. 20; stage IIIa unresectable 13 pts, IIIb 29, IV 63 (5 pts with asymptomatic brain mts). Evaluable for response (at least 3 c.s) 88 pts [6 had very early PRO, 16 stopped therapy because of tox (creatinine ≥ 1.6 mg/dL - 4 pts, cutaneous tox after fast dose G - 2 pts, subjective intolerance - 2 pts) and 2 because of cardiac failure not drug related]. Compliance by pts was good. No death therapy related occurred. Thrombocytopenia (thrp) WHO g 3–4 in 9.6% and 6.7% courses and 5 pts received plts transfusion; 3–4 neutropenia 27.7%; 45.2% pts received prophylactic or on-schedule G-CSF; g 3–4 anemia in 18.3% and 1.9%, 17 pts requiring blood transfusion. Non-haematological tox, except for the above reported: g 1–2 long standing peripheral neuropathy 20.2%. Objective responses: CR + PR 45 (51%, 95% C.I. 40–62); SD 30 (34.1%, 95% C.I. 24–45). Median response duration 6.5 *mo.s* (95% C.I. 3.5–13).

In conclusion, present report shows a 43.3% RR (CI 95%, 33.7–52.8) and a median overall survival 12.1 mo.s (95% C.I. 9.9–13.5), on an intention-to-treat basis (all pts included). Thrp and financial costs was much lesser than in the 3 accesses/c Others's regimens with P given on day 2.

EOLO (Eastern Oncology Lung Organization). In praise of GOCNE (Gruppo Oncologico Cooperative Nord. Est), CRO-Aviano (PN), and AOI (Associazione Oncologica Italiana), Aviano (PN), Italy.

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Gemcitabine (G) with concurrent chest radiation (XRT) followed by consolidation chemotherapy with gemcitabine plus cisplatin (CDDP): a phase I trial for patients with stage III non-small cell lung cancer (NSCLC)

F.V. Fossella[1], R.G. Zinner[1], R. Komaki[2], R. Lu[1], J.S. Lee[1], B.S. Glisson[1], K.M. Pisters[1], C.W. Stevens[2], J. Kelly[2], Z. Liao[2]. *[1] M.D. Anderson Cancer Center, Department of Thoracic/Head and Neck Medical Oncology, Houston, USA; [2] M.D. Anderson Cancer Center, Department of Radiation Oncology, Houston, USA*

We conducted a phase I trial to determine the maximum tolerated dose (MTD) of weekly G given concurrently with chest XRT for locally advanced NSCLC.

Eligibility: Medically inoperable stage II or stage III (except effusion) NSCLC, less than or equal to 5% weight loss, performance status 0-1 and no prior XRT or chemotherapy.

Treatment Plan: G weekly x 7 wks concurrent with chest XRT 63 Gy/35 fxs. Initial XRT used conventional 2D ports, but was modified to 3D conformal approach. With 3D XRT, G starting dose was 125 mg/m2/wk. 4 weeks after chemo/XRT is completed, patients receive consolidation chemotherapy consisting of 4 cycles of G at 1000 mg/m2/wk days 1, 8, and 15 plus CDDP 60 mg/m2 on day 1.