

a major factor in treatment decisions, our CE estimate of \$48,933 CAD (approximately \$30,583 USD) per LYG shows that treatment with DC in this setting is within an acceptable range of cost-effectiveness compared with other healthcare interventions.

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POSTER

# **A multi-institutional trial comparing survival of patients with brain metastases from lung cancer treated with temozolomide plus radiotherapy versus radiotherapy alone**

D. Antonadou<sup>1</sup>, N. Coliarakis<sup>2</sup>, M. Paraskevidis<sup>2</sup>, H. Athanasiou<sup>3</sup>, G. Sarris<sup>1</sup>, M. Synodinou<sup>1</sup>, G. Georgakopoulos<sup>1</sup>, C. Beroukas<sup>3</sup>, P. Karageorgis<sup>3</sup>, N. Throuvalas<sup>1</sup>. <sup>1</sup>Metaxa Cancer Hospital, 1st Radiation Oncol Dept, Athens, Greece; <sup>2</sup>Metaxa Cancer Hospital, 2st Radiation Oncol Dept, Athens, Greece; <sup>3</sup>Ag. Savas Cancer Hospital, 2st Radiation Oncol Dept, Athens, Greece

**Background:** This randomized study evaluated the efficacy and safety of concurrent administration of Temozolomide (TMZ) and WBRT compared to WBRT alone in patients with previously untreated brain metastases from lung cancer.

**Material and Methods:** Patients with histologically or cytologically proven lung cancer and brain metastases were randomly assigned to treatment with TMZ 75mg/m<sup>2</sup> per day during conventional WBRT 3 Gy /5days per week (total dose 30Gy) or with WBRT alone. Beginning one month post WBRT, patients in WBRT + TMZ received 200mg/m<sup>2</sup> per day for five consecutive days every 28 days for 6 cycles. The primary endpoint was radiological response assessed by CT scan or MRI at 3 months post WBRT. A survival analysis by treatment arm was also performed by different prognostic factors as number of lesions, first diagnosis brain metastases, recursive partitioning analysis (RPA) classes and cause of death (primary site and/or brain).

**Results:** To date 108 evaluable patients have been enrolled. The groups were similar with respect to age, gender, performance status neurological function score and RPA classes. 103 patients have been evaluated for response by radiological assessment (52 in the TMZ and WBRT group; 51 in the WBRT alone group). In the TMZ and WBRT group 48% of patients achieved complete and partial response compared to 27.5% respectively in WBRT alone group (p=0.031). Median follow up was 5.56 months (range 0.426-20.79). Median survival was 7.9 months in the TMZ plus WBRT and 4.3 in the control arm (p=0.06). The median survival in patients with multiple lesions in the study group was 7.3 months versus 4 months in the control group (p=0.1248). The median survival in patients with first diagnosis brain metastases and then lung was 7.4 months in the study group and 4 months in the control group (p=0.013). The median survival in RPA class I was 8 months in the TMZ and WBRT group compared to 8 months in the control group (p=0.78) and in Class II 3.8 months in the study group versus 3.31 in the control group (p=0.05). No grade 3 toxicities were noted.

**Conclusion:** These data indicate that combination treatment with TMZ and WBRT improves the efficacy of WBRT alone in brain metastases especially in chemotherapy naive patients.

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# **uPA and PAI-1 are associated with angiogenesis but not prognosis in non-small cell lung carcinoma**

B. Offersen<sup>1</sup>, P. Pfeiffer<sup>2</sup>, P. Andreasen<sup>3</sup>, J. Overgaard<sup>1</sup>. <sup>1</sup>Aarhus University Hospital, Department of Experimental Clinical Oncology, Aarhus, Denmark; <sup>2</sup>Odense University Hospital, Department of Oncology, Odense, Denmark; <sup>3</sup>Aarhus University, Department of Molecular Biology, Aarhus, Denmark

**Background.** Urokinase Plasminogen Activator (uPA) and Plasminogen Activator Inhibitor type 1 (PAI-1) has been suggested as a prognostic marker in non-small-cell lung carcinomas (NSCLC). This study investigates the levels of uPA and PAI-1 in 124 NSCLC, where estimates of tumour angiogenesis have been presented previously.

**Materials and methods.** uPA and PAI-1 levels were assessed in 119 and 123 frozen tumours, respectively, using a sandwich ELISA method.

**Results.** Median uPA was 30 ng/mg protein (range, 5-163 ng/mg protein), and median PAI-1 was 34 ng/mg protein (range, 3-286 ng/mg protein). uPA and PAI-1 were significantly correlated,  $P < 0.0001$ . Both factors were independent of histological type, T and N classification, malignancy grade, stage, age and vascular scores. Evaluated as continuous parameters or in tertiles, neither of the factors were markers of poor prognosis in univariate analysis. Significantly higher levels of uPA and PAI-1, respectively, were seen in tumours with an angiogenic vascular pattern as compared to

tumours with an alveolar vascular pattern. In multivariate analysis using overall death as endpoint, high disease stage ( $P < 0.0001$ ), old age ( $P = 0.05$ ) and adenocarcinoma ( $P = 0.002$ ) were identified as the only independent markers of poor prognosis, whereas the angiogenic vascular pattern was borderline significant ( $P = 0.06$ ).

**Conclusions.** In this study, significantly high uPA and PAI-1 levels were seen in tumours with an angiogenic vascular pattern as compared to tumours with an alveolar vascular pattern. However, neither uPA nor PAI-1 were prognostic markers in univariate or multivariate analyses. We conclude that uPA and PAI-1 are not prognostic markers in NSCLC, but may be involved in angiogenic processes in NSCLC.

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# **A pilot study of hyperfractionated accelerated radiotherapy (HART) following induction cisplatin and vinorelbine for stage III non-small cell lung cancer (NSCLC).**

S. Ishikura<sup>1</sup>, Y. Ohe<sup>2</sup>, K. Nihei<sup>1</sup>, K. Kubota<sup>2</sup>, R. Kakinuma<sup>2</sup>, H. Ohmatsu<sup>2</sup>, K. Goto<sup>2</sup>, S. Niho<sup>2</sup>, Y. Nishiwaki<sup>2</sup>, T. Ogino<sup>1</sup>. <sup>1</sup>National Cancer Center Hospital East, Radiation Oncology, Kashiwa, Japan; <sup>2</sup>National Cancer Center Hospital East, Thoracic Oncology, Kashiwa, Japan

**Background:** Continuous hyperfractionated accelerated radiotherapy (CHART) is superior to radiotherapy alone for inoperable NSCLC. The purpose of this study is to assess the feasibility and efficacy of HART (modified CHART) following induction chemotherapy for stage III NSCLC.

**Material and Methods:** Thirty patients with stage IIIA/B NSCLC were enrolled between July 1999 and March 2001. The treatment consisted of 2 cycles of cisplatin 80 mg/m<sup>2</sup> on day 1 and vinorelbine 25 mg/m<sup>2</sup> on day 1 and 8 every 3 weeks followed by HART; three times a day (1.5-1.8-1.5 Gy, 4-hour interval) for a total dose of 57.6 Gy in 36 fractions over 2.5 weeks. Patient characteristics: median age 64 (range 46-73), male/female: 24/6, performance status 0/1: 8/22, < 5% weight loss/5% or greater: 25/5, T1/2/3/4: 4/10/1/15, N0/1/2/3: 1/4/18/7, IIIA/B: 9/21, squamous/non-squamous: 13/17.

**Results:** All patients received 2 cycles of chemotherapy and all but one patient completed HART. Grade 3 or greater toxicities included neutropenia: 25, anemia: 3, thrombocytopenia: 2, infection: 5, esophagitis: 5, nausea: 3, radiation pneumonitis: 3, and dermatitis: 1. There were 2 early deaths due to radiation pneumonitis. The overall objective response rate was 83% (25/30, 95% CI: [65%, 94%]). With a median follow-up period of 33 months in surviving patients, the median survival time was 22 months (95% CI: [13, 34+]) and the 2-year overall survival was 50% (95% CI: [32%, 68%]). The median progression-free survival time was 10 months (95% CI: [8, 20]) and the 1-year progression-free survival was 47% (95% CI: [29%, 65%]). To date we have observed 2 cases with grade 3 subcutaneous tissue toxicity.

**Conclusions:** HART following induction cisplatin and vinorelbine was feasible and promising. Future investigation employing dose-intensified radiotherapy in combination with chemotherapy is warranted.

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POSTER

# **A phase II study of cisplatin (CDDP) and epirubicin (EPI) in malignant pleural mesothelioma (MPM). A study by the European Lung Cancer Working Party (ELCWP).**

T. Berghmans<sup>1</sup>, J.J. Lafitte<sup>2</sup>, B. Stach<sup>3</sup>, P. Recloux<sup>4</sup>, J. Lecomte<sup>5</sup>, C. Collon<sup>6</sup>, V. Ninane<sup>1</sup>, J. Klastersky<sup>1</sup>, J.P. Sculier<sup>1</sup>. <sup>1</sup>Institut Jules Bordet, Medicine, Bruxelles, Belgium; <sup>2</sup>CHU Calmette, Pneumology, Lille, France; <sup>3</sup>Cabinet Médical Dampierre, Pneumology, Anzin, France; <sup>4</sup>Clinique Saint Joseph, Medicine, Mons, Belgium; <sup>5</sup>CHU Charleroi, Pneumology, Charleroi, Belgium; <sup>6</sup>CHU le Raincy-Montfermeil, Pneumology, Montfermeil, France

**Background:** A meta-analysis of chemotherapy and immunotherapy in MPM showed that the most active chemotherapy regimen in term of response rate (RR) is a combination including CDDP and adriamycin (ADR) (Berghmans et al, Lung Cancer 2002; 38: 111). EPI demonstrated an activity similar to ADR (9% versus 11% RR) in regimens without CDDP. The aim of this study was to assess the RR and toxicity of CDDP plus EPI in MPM, a combination not reported in the literature.

**Material and methods:** Eligibility criteria included untreated unresectable MPM, adequate cardiac, renal, haematological and hepatic functions, absence of active infection and presence of assessable lesion(s). After central registration, patients received CDDP and EPI (both at 90 mg/m<sup>2</sup>), every 3 weeks for 3 cycles. Stable and responding (WHO criteria) patients were treated until best response or unacceptable toxicity. We used a two-stage optimal design of Simon to determine the number of patients to be