were mucositis (G3, 5 pts; G4, 1 pt), asthenia (G3, 2 pts), hand-foot syndrome (G3, 2 pts). G3/4 neutropenia occurred in only 5 pts (14%) (G3, 4 pts; G4, 1 pt). 8 pts required dose reductions. Enzymatic analysis in 12 pts to date suggests ratios of TP tumor/normal-tissue; TP/DPD in tumor and nuclear TS may be useful markers of response. Final data will be presented at the meeting. In summary, the combination of capecitabine and weekly docetaxel is well tolerated. PFS appears similar to every 3 weeks docetaxel, although RR appears higher and encourages evaluation of this regimen as a 1st line regimen in NSCLC.

P-212 Split-dose Cisplatin (CDDP) and Vinorelbine (VNR) in advanced non-small cell lung cancer (NSCLC): treatment outcomes including health-related quality of life (HRQL)

Christopher W. Lee[1], Nevin Murray[2], Kevin Murphy[1], Chris Williams[3], Mary V. MacNeil[4], Heidi Martins[4], Marianne Taylor[5], Amanda Jones[2], Kong Khoo[5], Barbara Melosky[2]. *[1] BC Cancer Agency, Surrey, Canada; [2] BC Cancer Agency, Vancouver, Canada; [3] BC Cancer Agency, Nanaimo, Canada; [4] BC Cancer Agency, Victoria, Canada; [5] BC Cancer Agency, Kelowna, Canada*

Background: Platinum-based chemotherapy remains the standard of care in treatment of advanced NSCLC although CDDP-related toxicity is a constant concern. A conventional means of minimizing CDDP side effects is to split the dose, which is not expected to alter efficacy.

Patients and Methods: From February 2000 to April 2002, fifty patients with advanced NSCLC were treated with CDDP 30 mg/m^2 and VNR 30 mg/m^2 IV on days 1 and 8 of a three-week cycle for up to 6 cycles. Ondansetron and Dexamethasone were prescribed routinely. HRQL was assessed at baseline, prior to each cycle, and in initial follow-up using the EORTC core questionnaire, QLQ-C30, and lung cancer module, QLQ-LC13.

Results: Patient characteristics were average age 63 years (median 64, range 37-79), male 23 (46%), ECOG 0-1 31 (62%), stage IV or recurrent disease 39 (78%), adenocarcinoma 21 (42%). The median number of cycles completed was 4 (range 1-6). Median survival was 256 days, with one-year survival 38%. CTC version 2 grade 3/4 toxicities included neutropenia 23 (46%), anemia 7 (14%), and thrombocytopenia 1 (2%). Four patients (8%) had febrile neutropenic episodes, 11 (22%) received blood transfusions, and 1 (2%) received platelet transfusion. There was no grade 3/4 renal dysfunction although grade 1/2 elevations in serum creatinine occurred in 11 patients (22%) necessitating dose modifications and/or delays. Compliance with HRQL assessments at each time point ranged from 78-100%. Rated as 'quite a bit' or 'very much' were nausea in 18/44 (41%), vomiting in 8/44 (18%), and tingling in the hands or feet in 8/44 (18%). By the end of the last cycle, 21/39 patients (54%) demonstrated a clinically significant greater than 10-point decline in global health status score compared to baseline, while 14/39 (36%) had stable or improved scores. Further analyses of HRQL outcomes will be presented.

Conclusions: Survival and toxicity with this schedule of CDDP and VNR are comparable to other established platinum-based regimens used in treatment of NSCLC. HRQL is also similar to results from recent randomized trials. Establishing that split-dose CDDP is associated with less CDDP-related toxicity and improves HRQL requires further study.

P-213 Phase II trial exploring gemcitabine and cisplatin as treatment of patients with non-small cell lung cancer (NSCLC) and inoperable brain metastases

Lionel Bosquee[1], Valerie Quadvlieg[2], Nicole Barthelemy[3]. *[1] EORTC, Liège, Belgium; [2] CHU LG, Liège, Belgium; [3] CHU Liège, Liège, Belgium*

Background: Brain metastases are frequent in NSCLC, either at diagnosis or during follow-up. Patients with inoperable metastasis are treated with whole brain radiotherapy (WBR) and have a poor prognosis, with median survival shorter than 6 months. Despite the availability of platinum-based chemotherapy, patients with brain metastases are often excluded from clinical trials, because it is considered that the blood-brain-barrier does not allow chemotherapy drugs to enter in the central nervous system (CNS). Yet, this has been refuted by some investigators. Therefore, the purpose of this study was to evaluate the efficacy of gemcitabine and cisplatin in the treatment of NSCLC patients with unresectable brain metastases.

Patients and methods: Patients with NSCLC and unresectable CNS metastasis were enrolled in this phase II study. All patients signed informed consent. Treatment consisted of gemcitabine 1000 mg/m^2 and cisplatin 50 mg/m^2, both delivered on days 1 and 8, every three to four weeks.

Results: 26 consecutive patients were enrolled in our institution. 22 had synchronous brain metastases and were chemotherapy-naïve. 4 patients were enrolled after brain relapse following previous chemotherapy (disease free interval: mean: 13.2 months, range: 9-26). Two patients were not evaluable because of early death, after 6 and 8 weeks, repectively. After 2 cycles, the documented CT scan response rate (RR) in brain metastases was 71% in 24 evaluable patients. After 4 cycles the RR was 73% in 15 evaluable patients. With 7 complete responses and 8 partial responses, the overall RR was 62%. One patient had stable disease. All but three of the responding patients had a response on their primary lung tumor lesion. The mean duration of response was 6.8 months and the overall mean survival is 5.4 months overall and 7,2 months in responding patients. Toxicity: no infection, no bleeding, no non-hemato toxicity > gr2 was seen; no particular CNS toxicity post radiotherapy was noticed (42% of the patients received WBR).

Conclusions: This chemotherapy regimen shows encouraging activity in NSCLC patients with CNS metastases. Further trials in patients with NSCLC and CNS metastases are warranted.

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P-214 Long-term remissions induced by oral Temozolomide in progressive, pre-radiotherapy treated brain recurrences from non-small cell lung cancer

Roberto Bordonaro[1], Carmelo Giannitto-Giorgio[1], Dario Giuffrida[1], Stefano Cordio[1], Giuseppe Lavenia[1], Placida Salice[1], Giuseppina Blanco[1], Laura Di Dio[1], Francesco Marletta[2], Salvatore Saita[3]. *[1] S. Luigi - S. Curro Hospital, Catania, Italy; [2] S. Luigi - S. Curro Hospital, Catania, Italy; [3] Thoracic Surgery - Vittorio Emanuele Hospital, Catania, Italy*

Brain recurrences from non-small cell lung cancer (NSCLC) are generally associated with poor-prognosis; the median survival (MS) after presentation do not exceed 3 to 4 months. Whole-brain radiotherapy (WBRT) represent the gold-standard treatment in this setting; it may induce only a modest improve in MS and do not represent a real chance of cure. There's actually no one standard therapeutic approach for those patients (PTS) who experience progressive disease after WBRT. Oral Temozolomide (TMZ) is a second-generation alkylating agent that showed efficacy against cerebral recurrences from various type of solid tumours. From 10/2000 we started a phase II study to assess the efficacy and the tolerability of TMZ, given orally at the dose of 200 mg/mq for 5 consecutive days in a 28-days cycle, in PTS affected by cerebral metastases from NSCLC that progressed after WBRT.PTS pretreated with almost one line of chemotherapy (CHT) for the primary tumour and/or extra-cerebral recurrences, with evaluable disease assessed by CT and/or MRI, ECOG-PS 0 - 3, and adequate hematological, hepatic and renal functions were considered eligible. Thirteen PTS entered onto the study; the median age was 65 years and the median ECOG-PS was 1. TMZ shown high tolerability in this subset of PTS, with no grade 3 or 4 toxicity registered. We performed a first analysis on may 2002; the overall response rate (ORR) was 61%, with two PTS that achieved a complete response (CR), and six stable disease, with a median survival of 7 months for the entire group. Among the responders PTS, the median duration of response (MDR) was 11 months. We recently updated our series; three PTS were still alive at 13, 16 and 22 months from the start of the therapy, respectively. Two of them have been experienced an extra-cerebral progression of the disease so they underwent salvage CHT based on docetaxel combined with TMZ; their brain metastases remain stable 2 and 6 months later the progression outside the central nervous system, respectively. Among the ten deceased PTS, we observed 8 progressive-disease-related deaths (80%) and 2 (20%) tumour-unrelated deaths in PTS who experienced post-radiotherapy-cerebral necrosis. Oral TMZ, alone or combined with other agents, is safe and well tolerated in this setting and may represent a valid therapeutic option in this poor-prognosis subset of PTS. It also seems able to induce long-term remissions in a small subgroup of PTS.

P-215 Analysis of xeroderma pigmentosum complementation group D (XPD) in the NATCH trial: a neoadjuvant/adjuvant paclitaxel/carboplatin trial in early non-small-cell lung cancer (NSCLC)

Enriqueta Felip[1], Bartomeu Massuti[2], Itziar de Aguirre[3], Guillermo Alonso[4], Jose Maestre[1], Antonio Torres[5], Manuel Rodriguez-Paniagua[2], Jose Maria Borro[4], Jose Javier Sanchez[6], Rafael Rosell[3]. *[1] Hospital Universitari Vall d'Hebron, Barcelona, Spain; [2] Hospital General de Alicante, Alicante, Spain; [3] Hospital Germans Trias i Pujol, Badalona, Spain; [4] Hospital Juan Canalejo, La Coruna, Spain; [5] Hospital Clinico San Carlos, Madrid, Spain; [6] Universidad Autonoma de Madrid, Madrid, Spain*

XPD takes part in the unwinding of DNA and forms a complex with the basal transcription factor TFIIH during transcription-coupled repair. Two functional polymorphisms in XPD (Lys751Gln and Asp312Asn) have been related to lung