*Treatment:* Pts were treated with P 3 h i.v. infusion after standard premedication on day (d) 1, IFO was given as 1 h i.v. infusion with the standard use of Mesna i.v. on d.2-5. The next cycle was given on d.22. Number of cycles depending on response and toxicity. We chose the following dose levels (dl): [mg/m$^2$] dl1: P 135/IFO 1500; dl2: P135/IFO 2000; dl3: P 175/IFO 2000; dl4: P175/IFO 1500. MTD was defined: neutropenia 4° longer than 5 days or febrile neutropenia, thrombopenia $\geqslant$3°, other organ toxicity >2° according to WHO criteria.

*Patient Characteristics:* 14 pts entered this ongoing trial. 13 pts entered dl1-3 and so far 1 pt dl4; age 52 yrs (37–66), WHO PS 1 (0–2).

*Pretreatment:* All pts had had a platinum based combination chemotherapy for advanced stage ovarian carcinoma prior to study entry. 10/14 pts had cisplatinum refractory disease with disease progression while receiving prestudy treatment. Number of prior treatment regimens 1.5 (1–3).

*Toxicity and Results:* With regard to P treatment, after standard premedication neither mild nor severe HSR's occurred. The following toxicities could be observed in 10 pts and 51 treatment cycles at dl's 1 + 2 [grade WHO (number of cycles)]: neutropenia 2° (6), 3° (21), 4° (24); anemia 2° (24), 3° (6); thrombocytopenia 1° (7), 2° (6); nausea/vomiting 1° (33), 2° (18); myalgia 1° (33); peripheral neuropathy 1° (36), 2° (12); mucositis 1° (39), 2° (8); diarrhea 1° (13), 2° (3). After we performed dose escalation of IFO up to 2000 mg/m$^2$ during dl 2 and 3 in 2 out of 8 pts treatment interruptions have to be performed because of CNS toxicity 3° WHO and in one additional patient suffering from nephrotoxicity grade 3 WHO. The MTD of IFO used in the combination with P and given over 4 days is 1500 mg/m$^2$. In order to enhance the efficacy of P we escalated the dose up to 175 mg/m$^2$ and intend to treat the following pts according to dl4. At all dl's responses could be observed. dl1 (5 pts): PR 2, SD 3; dl2 (5 pts): CR1, SD3, PD 1; dl3 (3 pts): CR1, PR2; dl4 (1 pt): not evaluable for response and toxicity so far.

*Conclusions:* The combination of P and IFO is leasable and active in the treatment of pretreated advanced ovarain carcinoma pts. Dl4 will be further evaluated during this ongoing study.

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## A PHASE II STUDY OF CARBOPLATIN AND HEXAMETHYLMELAMINE AS INDUCTION CHEMOTHERAPY IN ADVANCED OVARIAN CARCINOMA (AOC)

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The effect and feasibility of combination chemotherapy with carboplatin (C) and hexamethylmelamine (HMM) was evaluated on 27 patients with AOC. Two in FIGO stage IIC, 1 in IIIB, 8 in IIIC and 16 in stage IV. Carboplatin was given as 7 (GFR + 25) mg iv on day 1 and HMM 150 mg/m$^2$ orally on day 2–15, every 28 days. Three patients were not evaluable for response. Clinical response was seen in 17 patients (71%), with 6 (25%) complete and 11 (46%) partial responses. The median progression free survival was 15.6 months and the median cancer related survival 21.3 months. Four patients (15%) experienced grade 3 mental depression, none had peripheral neuropathy above grade 1. The hematologic toxicity was moderate, none had grade 4 leucopenia, but 4 (14%) had grade 4 thrombocytopenia. Carboplatin plus HMM had a high response rate with few side effects and a survival comparable to other platin based combinations.

506 POSTER

## EFFECTIVENESS OF TWO CISPLATIN-BASED DRUG COMBINATIONS IN THE TREATMENT OF ADVANCED OVARIAN CANCER

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The therapeutical effectiveness of two cisplatin-based drug combinations have been compared in a prospective trial with 83 advanced ovarian cancer patients. 39 patients received epirubicin-cisplatin (EP) combinations, whereas 44 patients were treated with a combination of cyclophoshamide-cisplatin (CP). Metoclopramide or 5-HT-3 receptor antagonists were used to control nausea and vomiting during therapy. The response rate to the cytostatic therapy was 71.8% (28 patients) in the EP group, and 84.1% (37 patients) in the CP group. There were no significant differences in the length of the progression free interval and in the survival rate either. The average survival times were 23 months and 21 months respectively. In the control of vomiting 5-HT$_3$ receptor antagonist (Navoban) is more effective.

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## A PHASE II STUDY OF TAXOL® (T) (PACLITAXEL) OVER 3 HOURS (H) IN 192 PLATINUM PRETREATED PATIENTS (PTS) FOR OVARIAN CARCINOMA (OC)

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*Eligibility criteria:* histologically proven OC, measurable/evaluable disease, relapse/progression after at least one platinum based CT, $\leqslant$ 3 prior CT. *Treatment:* 1 or 2 prior CT, T = 175 mg/m$^2$ [Group A (A) = 151 pts]; 3 prior CT, T = 135 mg/m$^2$ [Group B (B) = 41 pts] both by 3 hour IV infusion q 3 w. *Pts(192):* median (med) age: 57 yrs (25–72); PS 0 = 74 pts, PS 1 = 88 pts, PS 2 = 34 pts. nb prior CT : 1 = 81 pts, 2 = 73 pts, 3 = 36 pts. Toxicity (% cycles): 1184 evaluable cycles (cy) (983 in A, 201 in B) with a med nb per pt of 6 in A (1–21), 5 in B (1–11). *Cardiac tox.:* bradycardia: ($\leqslant$60 bpm) always asymptomatic = 13% (63 pts), hypotension ($\leqslant$90 mm/Hg) = 3% (24 pts), drop in systolic blood pressure $\geqslant$30 mm/Hg = 3% (23 pts). Out of 841 cy EKG 3% were abnormal (13 pts). *Minor hypersensitivity reactions (HSR):* 18% (A = 19%, B = 9%) in 73 pts, flushing (12%) and skin rash (4%). In 80 cy (7%) symptomatic treatment was required but never T discontinuation. No severe HSR occurred. *Hematologic tox.* induced treatment delay in 4% (A = 3%, B = 6%) and dose reduction in 1%. Gr 3–4 neutropenia: A = 32%; B =22%. Eleven pts experienced in 18 cy. any degree of fever of infection associated with a Gr 4 neutropenia, all in A. Thrombocytopenia Gr 3–4 = 1% (10 cy). Anemia Gr 3–4 = 3%, **Creatininemia** Gr 3 = 1 pt. **Liver Tox.** = 11 pts (6 with liver metastasis): ALP Gr 3–4 = 1%; ASAT Gr 3 = 0.3%. **Nausea/vomiting** Gr 1–2 = 13%.; Gr 3 = 2 cy. **Mucositis** Gr 1–2 = 4% all in A. **Paresthesias** (present in 45 pts at inclusion) Gr 1–2 : A = 43%, B = 28%, Gr 3: A = 5 cy. **Myalgias/arthralgias** Gr 1–2 = 18% (A = 20%, B = 7%) and Gr 3 in 3 cy. **Fatique** Gr 1–2 = 26%. **Edema** Gr. 1–2 = 6% and Gr 3 in 1 cy. No toxic death occurred. *Efficacy:* 185 evaluable pts, RR = 20% (CR = 5%, PR = 15%), SD = 32% (3 pts pCR). *Conclusion:* Taxol® given by 3 H infusion, is well tolerated. The RR seems not different from those observed with 24 H infusion.

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## COST EVALUATION OF TWO CHEMOTHERAPIES IN OVARIAN TUMOURS BASED ON A CONTROLLED CLINICAL TRIAL (CCT)

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Nowadays, the choice between two therapeutic schemes should not depend only upon treatment efficacy but also upon overall treatment cost including economic cost as well as time spent for treatment and nursing. A first evaluation of economic cost was performed on the first 24 patients (12 in each group) enrolled in a CCT comparing cisplatin (CDDP 100 mg/m$^2$, dl) and cyclophosphamide (CY 600 mg/m$^2$, d1) (CP arm) to carboplatin (CBDCA 300 mg/m$^2$, d1), CDDP (100 mg/m$^2$, d2) and CY (300 mg/m$^2$, d21) (CCP arm) to a total of 6 courses. Cost evaluation was limited to hospitalization, drugs, haematological and biological supplies that were induced by therapy. Financial evaluation was based on the actual cost for the institution during the 1992–1993 period. Results are expressed as the ratio of the cost induced by the CCP arm relative to that of the CP arm. The Wilcoxon rank sum test was used for comparisons.

*Results:* For hospitalization, the overall ratio was 1.5 ($P$ = 0.01), mainly based on an increase in days due to toxicity (ratio = 7.2, $P$ = 0.002); for drugs, the ratio was 10.0 ($P < 0.001$); it was 13.4 ($P < 0.01$) for haematological products (due to platelets transfusion, ratio = 53.4); for biological exams, the ratio was 1.5 ($P$ = 0.01). Overall, the overcost induced by CCP relative to CP was 11.2 ($P < 0.001$) when drug, haematological and biological expenses were considered. *Conclusion:* A second evaluation will consider additional costs (transportation or general practitioner help) and, above all, time spent by physicians as well as nurses. This approach should allow the calculation of the "cost by year of life won".