ments. The optimal sequence at the starting dose formed the basis for subsequent dose escalations.

Results: 15 patients have been enrolled over 10 months; median age 56, range 46–68; PS median 1, range 0–2; 2 FIGO stage Ic, 8 stage III, & 5 stage IV; 8 with grade 3 histology, 5 grade 2 & 2 grade 1. 2 patients had clear cell morphology. All had undergone 1 previous platinum-based regimen, with a median treatment-free interval of 5 mths, range 6 wks to 29 mths. Dose-limiting neutropenia (CTC IV) & ALT rise (CTC III) was encountered at gemcitabine 1000 mg/m^2 and paclitaxel 175 mg/m^2. 2 patients who received gemcitabine prior to paclitaxel on day 8 at dose level 1 (1000/135) developed grade 3 transaminase rise. No other sequence-specific toxicities have been identified, and no significant PK differences defined. Four out of 10 evaluable patients have so far achieved a partial response (UICC).

Conclusion: Gemcitabine MTD is being explored at paclitaxel 150 mg/m^2. Further work will be presented utilising paclitaxel day 1, gemcitabine day 1 and 8.

544 POSTER

Ifosfamide and Hexamethilmelamine as rescue treatment for cisplatin refractory ovarian cancer

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Purpose: Before the taxane clinical introduction, the drugs with >30% response rate used as second line treatment were Ifosfamide (*I*) and Hexamethilmelamine (*H*). No experience has been published yet with the *IH* combination. We describe the results of 21 patients (pts) with cisplatin refractory ovarian cancer.

Methods: pts received *I* 2.5 g/m^2 days 1–2, mesna 500 mg/m^2 iv hours 0 + 4 and 1000 mg/m^2 po hours 8 + 12 on days 1–2 and *H* 150 mg/m^2/day on days 3–16 every 28 days, on an ambulatory setting. Pts median age was 52 years (range 35–70); previous cisplatin/carboplatin based cycle number 4–10 (median 7).

Results: the overall response was 38% (8 pts) with 2 complete responses (9.5%), 5 pts with stable disease (23.8%) and 8 pts with progression (38%). Toxicity for 77 delivered cycles (3.6 median cycles/pt): neutropenia G0 = 39.5%, G1 = 27.6%, G2 = 17%, G3 = 12%, G4 = 3.9%; two episodes of trombocythopenia and anemia G1; other mild side effects: abdominal cramps, muscular pain, nausea, astenia. The DFS for CR was 14–19 months, the free-progression interval for PR was 4, 6, 7, 8, 8 and 9 months respectively. The median overall survival for the entire group was 13.3 months (range 3–31 months). The observed median dose intensity: *I* 1.14 g/m^2/week (91.2%) and *H* 481.55 mg/m^2/week (91.72%).

Conclusions: 1. the low toxicity profile allowed a 91% dose intensity in a heavily pretreated group of pts with poor known prognosis; 2. *IH* can be safely delivered in an ambulatory setting; 3. *IH* can be considered a good option for rescue treatment in cisplatin refactory OC due to a high response rate, a good palliative effect and survival impact. This combination deserves more experience in larger population.

545 POSTER

Paclitaxel (PX) – Carboplatin (CBP) versus cyclophosphamide (CTX)-carboplatin supported by G-CSF as first line chemotherapy in figo III–IV ovarian carcinoma (O.C.)

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Purpose: To evaluate and compare the efficacy and toxicity of the combination of PX-plus-CBP versus CTX-plus-CBP as first line treatment in advanced O.C.

Method: Sixty patients (pts) – so far – with measurable or evaluable disease, aged 55 (40–70), stage III 48 pts, stage IV 12 pts, were randomized to receive: PX 175 mg/m2 over 3 h and CBP 7 (AUC) or CTX 600 mg/m2 plus CBP 7 (AUC). Both arms were supported by G-CSF 5 μg/kg/day × 5 days.

Results: Thirty pts for each arm were eligible and evaluable for response and toxicity. In PX-CBP arm 27/30 pts (90%) (95% CL 74–98) responded with 3PCR, 15 CCR and 9 PR. In CTX-CBP 22/30 pts (73%) (95% C.L. 54–88) responded with 3 PCR, 10 CCR and 9 PR ($p < 0.18$). Peripheral neuropathy (100%) and alopecia were the main toxicities of the PX-CBP arm. Apart from 20% grade 2 thrombocytopenia in both arms there was no other hematologic toxicity. Disease progression during treatment was recorded in 3/30 and 8/30 of the two arms respectively.

Conclusion: PX-CBL combinations is highly active. Both regimen supported by G-CSF are very well tolerated. Survival is pending. Patient's accrual continues.

546 POSTER

Chemotherapy in advanced ovarian cancer (AOC)

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The study designs an optimising therapy strategy with platinum derivatives in the aim to obtain surgical reconversion and consolidation of the results in AOC. The data presented, were from 86 cases of epithelial AOC, stage III and IV followed up between jan. 1993–dec. 1996. Features of the cases: age 29–69, diagnosis by citology of ascites (36% of cases), or histopathology after laparotomy or anexectomy. All had locally-advanced disease. We performed: a) neoadjuvant chemotherapy with 3–4 CAP schedules (CDDP 75 mg/m^2 or carboplatinum 450 mg + cyclophosphamide 500 mg/m^2 + farmorubicine 75 mg/m^2); b) debulking or radical surgery and c) 6 CAP schedules q 3 weeks. In 65% of cases radical histerectomy, bilateral anexectomy and omentectomy was possible; 35% of cases underwent citoreduction. Correct hydratation and antiemetic treatment realized good tolerance. Disease free survival (DFS) obtained was 6–11 months with good quality of life (QOL). After 12–24 months 35% of patients were submitted to second look: 55% had CR, 30% had restant tumors <2 cm and 15% progressive disease. For the last two categories we repeated chemotherapy with 3–4 CP courses (cyclophosphamide 500 mg/m^2 + CDDP 100 mg/m^2 or carboplatinum AUC 6). Overall response was 76% with good QOL. The 4 years follow-up underlines the value of platinum based regimens in the treatment strategy of AOC, realizing better DFS and good QOL.

547 POSTER

Serum concentrations of soluble interleucin-2 receptors (sIL-2R) in patients with benign and malignant ovarian tumors

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Purpose: In sera of patients with several benign and malignant diseases soluble interleucin-2 receptors (sIL-2R) are found in sometimes very high concentrations. We wanted to investigate if measurement of sIL-2R in serum could be useful for differentiation between benign and malignant ovarian tumors.

Methods: In sera of 130 patients with benign ovarian tumors and 112 ovarian cancer patients at different FIGO-stages concentration of sIL-2R was measured preoperatively with a chemolumineszenz assay.

Results: sIL-2R serum concentrations in patients with benign diseases were between 197 and 3236 U/ml (median 573 U/ml), in those with ovarian cancer between 237 and 6230 U/ml (median 807 U/ml). An upper normal level of sIL-2R serum concentration in patients with benign ovarian tumors was defined at the 95th percentile (1200 U/ml) of the distribution of sIL-2R concentrations in these patients (cut-off). 33% of the ovarian cancer patients had sIL-2R concentrations above these cut-off. sIL-2R concentrations increased with FIGO-stage

Conclusion: We conclude that sIL-2R could become a new interesting tumor marker in ovarian cancer. Further studies should clarify the possibility of therapy monitoring by serial sIL-2R measurement.

548 PUBLICATION

Evidence of p*53*-independent activation of bcl-2 in advanced ovarian and endometrium carcinomas

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Purpose: p*53* and bcl-2 are important determinants of apoptosis. Inactivation of p*53* by mutation often results in high expression of bcl-2 that is known to block apoptotic pathways and may thus lead to chemo- or radioresistance. However, bcl-2 may also be activated by p*53*-independent mechanisms which are not fully understood. This study was initiated to evaluate the coexpression of p*53* and bcl-2 in advanced human epithelial ovarian (EOC) and endometrium carcinomas (ENC).

Methods: A total of 24 samples derived from patients advanced EOC (n = 18) or ENC (n = 6) were studied by immunohistochemistry. Antigen recovery