With increasing experience it was found that a combination of domperidone, dexamethasone & chlorpromazine at night controlled this toxicity in most pts. G 2 anaemia but not G 3 or 4 was seen in 5, G 2 or 3 neutropenia in 2 and G 1 & 3 thrombocytopenia in 2 pts. G 1 neurotoxicity was seen in 5 and G 2 in 6. Median treatment free interval was 12 mo. Responses [CR + PR] were seen in 15 (39%) [95% CI 24–55] of those evaluated according to EORTC & in 16 [36%] [95% CI 21–50] of those evaluated according to CA125. Overall response rate was 22 of 53 [42%] & was related to treatment free interval, 6 to 12 mo 32%, >12 to 24 mo 60% and >24 mo 57%. Median duration of response was 8 mo. Oral Hexalen is a highly efficient & well tolerated agent in pts relapsing after previously responsive ov ca. Response evaluation by a strict CA125 definition gives similar conclusions regarding efficacy of Hexalen to the EORTC criteria.

514 POSTER

H-CAP REGIMEN RESULTS IN LONG TERM SURVIVAL IN OVARIAN CANCER

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Clinical trials of Hexalen® (altretamine, hexamethylmelamine) in combination with cyclophosphamide, doxorubicin and cisplatin (H-CAP) as first line therapy for patients with advanced ovarian cancer were conducted at Vanderbilt University. Patients received 6 monthly courses of Hexalen (H), 150 mg/m^2 po days 1 to 14, cyclophosphamide (C) 300 mg/m^2 iv days 1 and 8, doxorubicin (A) 20 mg/m^2 iv days 1 and 8 and cisplatin (P) 60 mg/m^2 iv day 1. The survival data from this cohort of 55 patients were compared with those of a subsequent cohort of 22 patients treated with the identical dose and schedule of C, A and P. Results demonstrate a statistically significant survival benefit for H-CAP relative to CAP despite poorer prognostic characteristics: 36% of H-CAP patients had ≤3 cm residual disease vs 86% of CAP patients. Median survival for H-CAP patients was 45 months vs 29 months for CAP patients (P = 0.006). For patients with <3 cm residual disease, median survivals were 101 months for H-CAP vs 32 months for CAP; 45% of these H-CAP patients are alive at 9 years vs 10% of these CAP patients (P = 0.003). The addition of Hexalen to CAP resulted in significantly improved survival but no increase in toxicity. Hexalen warrants further evaluation as part of first line combination regimens for advanced ovarian cancer.

515 POSTER

PHASE II STUDY OF CISPLATIN (P), VINBLASTINE (V) AND BLEOMYCIN (B) IN RECURRENT OR ADVANCED DYSGERMINOMA (D)

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Dysgerminomas account for 1% of all ovarian cancers and 50% of all ovarian germcell malignancies. Half of the pts can be cured with local treatment. Eighteen pts with advanced D were entered in this study. Age 27 (range 13–48) yrs. Seventeen had prior surgery, one prior radiotherapy (RT). Delay since initial diagnosis was median 11 weeks. PS 12:0, 3:1, 3:2. Three had only a local recurrence; all others also metastatic disease. Treatment consisted of P 20 mg/m^2 d 1–5, V 0.15 mg/kg d 1,2, B 30 mg d 2,9 and 16 q 3 wks. Twelve pts obtained a CR (66%), five a PR (27%) and one could not be evaluated since immediate RT followed the CT. Of 18 pts 14 are alive and well, four died: 2 of progressive disease, 2 toxic death (one of septicaemia in leucopenia and one of lung fibrosis). Eighteen pts had 4 cycles, one 3, one 5 and one 6. Toxicity was as usual for this regimen: gr 3–4 leucopenia 78%, thrombocytopenia 17%, N&V 33% and alopecia.

Conclusion: PVB is a very active regimen in adv. D. with an overall RR of 93% and a 77% rel. free survival after 3$^+$ yrs.

516 POSTER

RHIL-3 AND G-CSF VS G-CSF ALONE AFTER TAXOL-IFOSFAMIDE-CISPLATIN (TIC) CHEMOTHERAPY (CT) IN RESIDUAL/PROGRESSIVE OVARIAN CANCER (OC)

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Treatment of residual or progressive OC after 1st-line CT remains unsatisfactory. A study was designed to test a new CT-regimen for this group of pts, furthermore, bone marrow protecting properties of a combination of rhIL-3/G-CSF vs G-CSF alone were evaluated. CT consisted of iv TIC chemotherapy (T: 135 mg/m^2 d1, I 1200 mg/m^2/d, d2–4 and C 30 mg/m^2/d, d2–4), in cycles without grade IV hematological toxicity taxol dose escalation was performed. Pts were randomized to arm A: rhIL-3 (10 μg/kg/d sc, d5–9) and G-CSF (5 μg/kg/d sc, d7–16) or arm B: G-CSF (as in A) alone. Four cycles (q21d) were scheduled. Until now 14/16 pts are evaluable for toxicity and efficacy. Nausea, vomiting and malaise were frequently observed in both arms, flu-like symptoms in 6/8 pts (A) vs 1/6 (B). Reversible peripheral neuropathy between cycles was reported in 4/8 pts (A) vs 3/6 (B), long-lasting peripheral neuropathy in 3/8 pts (A) vs 0/6 in (B). One pt (A) developed venous thrombosis, which reoccurred after rhIL-3. One pt (B) was hospitalized for bleeding in liver metastases. 65% of the cycles were 3-weekly (A) vs 50 (B). Grade IV neutropenia occurred in 27% of the cycles (A) vs 13 (B). Grade IV thrombocytopenia was observed in 50% of the cycles (A) vs 13 (B, P = 0.03). Platelet recovery tended to be faster in arm A. Tumor responses were achieved in 4/8 pts (A) vs 4/6 (B), a 57% overall response rate. TIC offers a promising regimen in residual and progressive OC after 1st-line CT. Synergistic effects of rhIL-3/G-CSF were limited with regard to platelet nadir, but platelet recovery was faster.

517 POSTER

CLINICAL (WHO) AND SERUM TUMOR MARKER (CA125) RESPONSE TO PLATINUM BASED CHEMOTHERAPY AFTER TREATMENT WITH PACLITAXEL IN PATIENTS WITH OVARIAN CANCER (OVCA)

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Background: At present, 60% to 90% of the patients (pts) with OVCA demonstrate objective responses to first-line platinum (Pt)-based combination chemotherapy (CT). Serial CA 125 measurements reflect the clinical course of the disease in these circumstances correctly in 89% of the cases (Neth J Med 40:36, 1992). In pts treated with paclitaxel (Taxol®, T) after Pt-based CT this correlation is poor (Proc ECCO-VII; 133, 1993). The question can be raised whether this poor correlation is a general phenomenon in relapsed OVCA pts or whether this is related to the use of T.

Objectives: to determine clinical response and CA 125 response with Pt-based CT after T treatment and to assess the correlation of serum CA 125 levels with the clinical course with both treatments, i.e. with T and with Pt-based CT after T.

Methods: Doubling or halving of CA 125 levels were considered to be a significant increase or decrease. For the relationship with the clinical course we used the Spearman rank correlation.

Results: So far, 18 pts (with 6/18 clinical responses and 15/16 marker responses on T) were pre-treated with a Pt-based CT, 9 in 3rd-line, 6 in 4th-line, and 3 in 5th-line. 7 Pts responded (39%; 2 CR, 5 PR) according to WHO criteria and 8 of 15 evaluable pts (53%) had a CA 125 response. The correlation between changes in CA 125 levels and clinical course was poor for T (correlation 0.27; P = 0.31), but significant for Pt-based CT (correlation 0.67; P = 0.0066).

Conclusions: 1) Pt-compounds and T are not cross resistant 2) the poor correlation between changes in serum CA 125 levels and the clinical course of the disease seems to be specific for treatment with T.