patient refractory to either platinum or taxane. Grade 4 neutropenia occurred in 48% and febrile neutropenia in 17%. Two septic deaths occurred during treatment (1 patient receiving 1.25mg/m2 over 5 days, 1 patient receiving 1.5mg/m2 over 5 days). Twenty seven percent (11) patients experienced dose delays (7of whom received 1.5mg/m2 dose) and 17% (7 patients) had a dose reduction (4 of whom received 1.5mg/m2).

Conclusions: The response rate is lower than was anticipated and is likely to be a function of dose delays and reductions, and the high frequency of platinum and/or taxane-refractory disease. Our data suggest that the optimal use of topotecan in the off study salvage setting is in minimally pre-treated, fit patients at a dose level of 1.5mg/m2 over 4 or 5 days. Randomised studies comparing topotecan with less toxic alternative therapies (such as oral VP16) in this setting are warranted.

1185 POSTER

Efficacy and toxicity of chemotherapy (Carboplatin/Ifosfamide) combined with whole body hyperthermia (WBH) in patients with recurrent ovarian cancer - a phase II study (dolphin-1-study)

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Purpose: Despite several improvements in the cytostatic treatment over the last years, the prognosis of patients with recurrent ovarian cancer still remains unfavorable. There is some evidence that the combination of whole body hyperthermia (WBH) with special cytostatic agents (e.g. carboplatin, ifosfamide) leads to a higher efficacy through increased cellular metabolism and immunostimulation.

Methods: In an ongoing prospective multicenter phase II Study we are evaluating the toxicity and efficacy of 11 patients (38 treatment courses) with recurrence of ovarian cancer receiving WBH (target temperature 41.8°Celcius over 1 hour) combined with carboplatin AUC5 and ifosfamide 3g/m2 every 28 days, for 6 cycles or until progression. Patients (=65 years) are required to have sufficient cardiac, pulmonal and renal function.

Results: Toxicity lead to dose reduction in 14 courses (36,8%). The following toxicities (NCI) were seen: myelotoxic side effects as grade 3 leucocytopenia in 11 cases (28,9%) and grade 4 leucocytopenia in 6 cases (15,8%). Thrombocytopenia grade 3 occurred in 9 courses (23,7%), grade 4 in 7 courses (18,4%). In 2 courses renal toxicity grade 2 appeared. In 10 courses (26,3%) skin burnings grade 2 and in 4 courses (10,5%) skin burnings grade 3 were reported. No other severe treatment related adverse events were noted. Preliminary data on efficacy include 5 patients with partial remission, 4 patients with stable disease and 1 patient with progression.

Conclusion: The combination of carboplatin and ifosfamide with WBH is well tolerated and appears to be feasible and safe. After the successful completion of the phase II sequence (15 patients) the study will continue as a randomised multicenter phase III study, comparing above treatment with normothermic cytostatic application. This will be the first phase III trial to evaluate the efficacy of WBH combined with chemotherapy.

1186 POSTER

Chemotherapy with carboplatin/docetaxel for primary and recurrent epithelial ovarian cancer

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The high incidence of peripheral neurotoxicity associated with platinum/paclitaxelcontaining chemotherapy for ovarian carcinoma is frequently a limiting factor with respect to long term treatment. A pilot study was conducted with docetaxel instead of paclitaxel to investigate if incidence of neurologic toxicities could be decreased withoutcompromising tumor response.

Sixty-one pts with epithelial ovarian cancer (FIGO II-IV), were treated with the combination of carboplatin (AUC 5) and docetaxel (75mg/m2), i.v., q3w. Twenty-nine pts received 6 courses of carboplatin/docetaxel as first-line treatment for ovarian carcinoma. A further 32 pts were treated with carboplatin/docetaxel for relapse >12 months as second line therapy.

A total of 300 courses was administered: Predominant WHO grade 3/4 toxicity was leucopenia (21/61). Grade 3 thrombocytopenia occurred in 5% of pts. No Grade 3 neuropathy was observed,. Grades 2 and 1 neuropathy was seen, respectively, in only 2/61 pts and 16/61 pts. In the second-line cohort, neurotoxicity was not increased. 12/61 pts complained of mild to moderate fluid retention, mild to moderate nausea and vomiting (WHO 2/3) occurred in 24/61 pts. No ototoxicity was observed.

Of 26 first-line patients evaluable for response, ORR (CR + PR) was 79%. Thirty second-line pts were evaluable for responsewith ORR of 75%. Calculated median TTP for first-(23/29) and second-line cohorts (23/32) was 10 and9,4 mos, respectively.

In summary, the observed efficacy of carboplatin/docetaxel combination therapy for ovarian carcinoma is comparable to that reported for platinum/taxane combinations. Nevertheless toxicities, particularly neurologic side effects are less severe and less predominant with carboplatin/docetaxel.

1187 POSTER

Complement activation in ovarian cancer

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Background: Activation of the complement system plays a key role in the inflammation process and in protecting the host from pathogenic agents, e.g. viruses and bacteria. Complement activation has also been observed in connection with neoplastic disease. The aim of the present study was to determine whether complement is activated in patients with cystic ovarian tumors and if the degree of activation differs in malignant and benign tumors.

Methods: C4d, Factor Bb, C3a/C3a-desArginine and SC5b-9 were measured in 65 patients with lower abdominal cystic ovarian tumors, including 31 ovarian cancers and 35 benign ovarian tumors. Patient age and tumor size did not differ significantly between the two groups. The levels of C4d, Factor Bb and SC5b-9 were determined in plasma, in ascites and in cyst fluid with Enzyme Immune Assay (EIA) methods. Levels of C3a/C3a-desArginine were determined in the same compartments with an ELISA procedure.

Results: C4d and C3a/C3a-desArginine were significantly elevated in plasma, ascites and in cyst fluid in patients with malignant ovarian tumors compared to patients with benign tumors. Factor Bb and SC5b-9 showed significantly higher levels in plasma and in cyst fluid in patients with malignant cystic ovarian tumors compared to those with benign tumors.

Conclusions: This study shows that complement is activated in patients with ovarian cystic tumors. There is a significantly higher grade of activation in patients with malign ovarian tumors than in patients with benign cystic tumors in the ovaries.

1188 POSTER

Long-term survival with consolidation intraperitoneal chemotherapy (IP) in advanced ovarian cancer (AOC) with complete pathological remission

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Intraperitoneal (IP) chemotherapy (CT) in AOC demonstrated significant activity in patients with small-volume residual disease (RD), as part of the initial chemotherapy or after failure of IV CT. However, long term evaluation is seldom reported. We report our results with consolidation IP CT in patients who achieved a complete pathological response after IV CT. This study included patients (pts) with AOC (stage III-IV, under 70 yrs) who entered in four prospective trials (1984-1997) including IV CT based on cisplatin (6 cycles) and anthracyclines, early debulking surgery after three cycles of CT in case of initial RD over 2 cm, second-look laparotomy (SLL) and intraperitoneal consolidation CT (Proc ASCO; 10:639, 1991; Proc ASCO; 12:888, 1993; Eur J Cancer; 28:53, 1992). Among 219 pts, 68 with biopsy negative second-look laparotomy received every 4 weeks 3 consolidation cycles of IP CT via a totally implantable port. Fifty six patients received mitoxantrone 25 mg/m2 D 1, VP16 120 mg/m2 D 1. In 16 pts, IP cisplatin 100 mg/m* was added (no previous neuropathy). Nine patients received high dose cisplatin (200 mg/m*) and 3 patients had cisplatin 200 mg/m*+cytarabine 2g. Only 13 pts (19%) did not receive the full 3 cycles.