Methods: This guideline advised chemotherapy with cyclophosphamide 750 mg/m^2 (C) and cisplatin (P) 75 mg/m^2 i.v. q21 days for OC FIGOstage IIb with macroscopic tumor rests to IV and with melphalan (M) 0,2 mg/kg p.o. d1-5 q28 days for stage I to IIb (except Ia well differentiated and IIb with macroscopic tumor rests). From the regional cancer registry 37 patients were found treated for OC from 1992 to 1995.

Results: 13 patients were eligible for M, 4 of them did not receive chemotherapy at all, 1 received M and 8 received CP, 22 patients were eligible for CP. They all had chemotherapy but alternative schedules as C adriamycin (A) P or C carboplatin (Ca) q 21 days were given. In total 182 cycles were given: 5 M, 143 CP, 26 CAP and 8 CCa. Excluding M treatment, 155 cycles were longer than 22 days. Median duration per cycle was 25 (range 20–34) days. Important reasons for delay were bone marrow toxicity (WBC < 3 or Platelets < 100), 26 cycles with lab control on day 20–22, 46 cycles with lab control <20 days after last chemotherapy, and hospital logistics, 53 cycles. Median total DI (tDI) defined as given dose/intended dose for all CP, CAP and CCa cycles given was 0.96 (range 0.73–1.03)), reasons for dose alterations were calculation faults, and no dose reduction as advised in the guideline when 3 ≤ WBC < 4. The relative DI (rDI) defined as tDI × number of cycles × 21/actual duration of therapy median was 0.79 (range 0.48–0.89). 7 of 30 patients had a rDI > 0.85.

Conclusion: rDI is considerably affected by delay, due to guideline violations as hospital logistics, time of lab control and no dose reductions as indicated. These are important factors interfering with optimal treatment outside a study protocol, even when a guideline is used.

941 POSTER

A combination of a fixed dose of carboplatin plus paclitaxel and adriamycin in first line therapy for advanced ovarian cancer and suboptimal surgical cytoreduction. A phase I trial of the Spanish group for ovarian cancer research and treatment (GEICO)

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To develop a tolerable treatment of carboplatin at a fixed dose (AUC = 5) plus paclitaxel, given in 1 hour, and adriamycin every 21 days, the GEICO group carried out a phase I trial. Inclusion criteria were: histologically confirmed ovarian cancer, PS < 3 and normal liver, kidney, heart and marrow function. Patients after initial surgical debulking were included in 5 consecutive levels of dose:

Level 0 consisted in Paclitaxel 135 mg/2 and Adriamycin 40 mg/2. Level 1 rised adriamycin up to 50 mg/2 and mantained paclitaxel at the same dose than level 0. Level 2 went up to 150 mg/2 of paclitaxel and kept adriamycin at 50 mg/2. Level 3 rised again paclitaxel to 175 mg/2 and kept adriamycin at 50 mg/2. Level 4 was planned at the same previous dose of paclitaxel and adriamycin was given at 60 mg/2. From November-97 to September-98, 23 patients were accrued in 5 different institutions. Mean age was 61 (41–73). Three patients were respectively included at dose levels 0, 1 and 2. At dose level 3 8 cases were registered and 7 were accrued at dose level 4. Carboplatin was given at a dose calculated by the Calvert's formula at AUC = 5. Dose limiting toxicity was assessed after the first course of therapy and was febrile neutropenia at dose level 4. No other non hematological toxicity was detected as limiting. One patient at dose level 2 and 3 at dose level 4 had neutropenic fever. Level 4 was considered Dose limiting toxicity and the dose level 3 was the recommended dose for further phase II trials.

942 POSTER

Cytokines IL-1b, IL-2, IL-6, IL-8, MCP-1, GM-CSF and TNFa in patients with epithelial ovarian cancer and their relationship to treatment with paclitaxel

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In-vitro work suggests that cytokines may be important modulators, both of the cytotoxic effects of paclitaxel and subsequent drug resistance. This has been investigated in-vivo in women with ovarian cancer. ELISA was utilized to evaluate the expression of 7 cytokines in serum and peritoneal fluid. This included 12 paired samples of serum and peritoneal fluids from post operative patients and serum from an additional 18 women with ovarian cancer. Samples were taken prior to, 24 hours after and approximately 7 days after treatment with paclitaxel. Serum concentrations of the cytokine IL-6 and the chemokine IL-8 were elevated in women with ovarian cancer in comparison to healthy controls ($p < 0.05$). There was no increase in the expression of IL-1b, IL-2, GM-CSF or TNFa in either serum or peritoneal fluid. Peritoneal fluid concentrations of IL-6, IL-8 and MCP-1 were two to three logs greater than those in serum. Serum concentrations of IL-6 and IL-8 were associated with the response to chemotherapy. Raised concentrations of IL-6 correlated with a poor final outcome ($p = 0.039$) and raised IL-6 and IL-8 correlated with a poor immediate response to chemotherapy ($p = 0.041$ and $p = 0.041$ respectively). MCP-1 did not correlate with treatment outcome. There was a relatively clear pattern of change in all three cytokines. In serum, IL-6, IL-8 and MCP-1 decreased with the administration of steroids prior to paclitaxel, and increased in the 24 hours after paclitaxel. Levels in peritoneal fluid tended to decrease in the 24 hours after paclitaxel. Post operative drainage fluid was relatively acellular preventing flow-cytometric analysis of epithelial cells for apoptosis, but suggested activation of T cells by paclitaxel, particularly an increase in CD25+4+ cells. IL-6 and IL-8 appear to be of prognostic importance in epithelial ovarian cancer. Treatment with paclitaxel is associated with upregulated expression of a limited number of cytokines in women with ovarian cancer, notably IL-6, IL-8 and MCP-1.

943 POSTER

Tumor angiognesis, hepatocyte growth factor, and c-Met expression in endometrial carcinoma

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Purpose: This study was designed to evaluate the significance of tumor angiogenesis and angiogenic factors such as hepatocyte growth factor (HGF) and c-Met in endometrial carcinoma.

Methods: To evaluate tumor angiogenesis, the microvessels within the primary endometrial carcinoma were highlighted by immunostaining their endothelial cells for yon Willebrand factor. HGF and c-Met expression were identified with specific antibodies. The correlation between these factors and prognosis were analyzed in 93 patients with endometrial carcinoma.

Results: A high microvessel count (>110 in a 0.90 mm2 area) was significantly correlated with stage III and IV, G3, positive lymph node involvement, and shorter survival, c-Met was significantly correlated with stage III and IV, G3, and shorter survival. HGF was significantly correlated with stage III and IV. Multivariate analysis showed that stage III and IV, G3, myometrial invasion >1/2, and a high microvessel count were independent indicators.

Conclusions: Microvessel count and c-Met expression were significant prognostic indicators for patients with endometrial carcinoma.

944 POSTER

Neoadjuvant chemotherapy (NC) in patients with locally advanced cervical cancer (LACC)

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Purpose: To investigate the impact of NC in the operability rate, local control, progression free survival (DFS) and overall survival (OS) in patients with LACC.

Methods: Inclusion criteria was unresectable stage IB2-III cervical carcinoma diagnosis. Treatment consisted of two cycles of Cisplatinum 50 mg/m^2, bleomicin 30 mg and ifosfamide 5 gr/m^2. Patients considered to be resectable after chemotherapy underwent a type II radical abdominal hysterectomy and postoperative radiation therapy. Those considered not to be resectable were treated with radical radiotherapy.

Results: Fifty four evaluable patients were included in the study. Median follow-up time was 41 months (range, 26–165). Clinical responses were observed in 34 (64%) out of 54 patients: CR was in 2 (4%) patients and PR in 32 (59%). Seventeen (31.5%) had disease stabilization and 3 (5.5%) progressed. Fifty percent of patients underwent radical surgery (6 out of 7 (85%) stage Ib2, 3 (100%) out of 3 stage IIa, 17 (63%) out of 27 stage IIb and 1 (5%) out of 17 stage IIIb). Median DFS was 96 months for the group treated with radical surgery versus 60 months for the rest of patients ($p = 0.009$). Median OS was no reached in patients undergoing surgery versus 42 months in those not resected ($p = 0.005$).

Conclusions: NC is active in LACC allowing radical surgery in a high percentage of patients. The potential benefit of this strategy respect to radiotherapy alone should be investigate in prospective randomized trials.