(<1/2) G1 = 29%, G2 = 20%, G3 = 8%, I stage = 54%, II stage = 4%; for volume (>1/2)) G1 = 11%, G2 = 19%, G3 = 27%, I stage = 30%, II stage = 12%. In the (<1/2) group 63% of the patients did not received RT, in the other 32%.

Results: In the whole group, relapses were 16.4% (local 8.7%, distant 6.8%, both 0.9%). The incidence of the local relapses (<1/2) vs (>1/2) is 5% vs 11%, distant relapses 3% vs 11%, NED survival after 60 months is 92% vs 73% (p = 0.0001).

The most important prognostic factors using multivariate analysis are: for Local relapse Vol. >1/2; for Distant relapse G3, Vol. >1/2, stage II; for Mortality G3, Vol. >1/2. Radiation therapy decreases significativaly the risk for local relapse

Discussion: in our series tumoral volume seems to be a very important prognostic factor influencing relapse and mortality rates, as showed in the table. Further studies are required to confirm these data, especially using more precise and rigorous criteria in anatomo-pathological analysis.

932 POSTER

8-hydroxydeoxyguanosine in cervical cells DNA: Correlation with HPV infection and grade of dysplasia

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In this study, the 8-OhdG level was assessed in human cervical cells by an immunoperoxidase method and was related to the presence of HPV infection and dysplasia. After optimising the immunohistochemical method in detecting oxidative DNA damage by testing it on AFB1 treated MCF-7, we have used this technique to estimate the oxidative damage in cervical cells collected during a routine PAP tests. 38 women (age range: 20–55, mean age 36.8, s.d. 9.6) were enrolled into the study. After informed consent was obtained, cervical cells were spread on slides precoated with 0.2% poly-D-lysine. Quantitation of specific nuclear staining in AFB1 treated MCF-7 confirmed the ability of the method to detect and differentiate between different damage in a linear dose-related fashion. The analysis of variance (ANOVA) of the data from human samples showed significant differences in standard deviation of the 8-OHdG level between normal, low grade and high grade of dysplasia (p < 0.0001). Comparing the three groups, statistically significant differences were detected between normal and high grade dysplasia (p < 0.001, Bonferroni corrected) and between low grade and high-grade dysplasia (0.003, Bonferrroni corrected), whereas non statistically significant resulted the difference between normal and low grade dysplasia (p = 0.174, Bonferroni corrected). Grouping observations by HPV status, no significant difference was detected in 8-OHdG levels between HPV+ and HPV− subjects (p = 0.8767). The ordered logistic regression analysis showed that while at low 8-OhdG levels the probability of dysplasia was higher for HPV+ subjects, at high 8-OhdG levels the probability of presenting a dysplasia was similar in both HPV− and HPV+ subjects. In conclusion, the immunoperoxidase method, applied to single human cervical cells, provides clear evidences that significant differences exist in 8-OHdG content between normal and dysplastic cells and that oxidative DNA damage might be able to promote cervical carcinogenesis independently by HPV status.

933 POSTER

Phase I study of topotecan (T) with carboplatin (C) alternating with paclitaxel (P) via 3 hour infusion with carboplatin (C) in treatment of newly diagnosed ovarian cancer (OC)

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Objective: Myelosuppression has made it difficult to incorporate T into a triplet with P and a platinum. This study was designed to find the maximum tolerated dose (MTD) of T in combination with C. Alternate cycles of P and C were given to gain exposure to all three active agents.

Methods: C (AUC 5 or 4) was administered first on Day 1 followed by T (0.75 mg/m^2 × 5 days for the first cohort of patients. Due to grade 4 thrombocytopenia, T was reduced to 0.6 mg/m^2 × 3 days and then re-escalated in subsequent cohorts) in cycles 1, 3, 5, and 7. P (175 mg/m^2) was given over 3 hours, then C on Day 1 of cycles 2, 4, 6, and 8. All cycles were to be at 21-day intervals. Dose limiting toxicity (DLT) included: ANC < 500 for >5 days, or grade 4 neutropenia with fever (>38.5 C), platelet count <10,000 or <25,000 with associated bleeding, delay of >7 days in recovery, or non-hematologic toxicity ≥Grade 3. If 1 of 3 patients had a DLT, another 3 were added. If DLT was due to neutropenia or delay in recovery of ANC, granulocyte colony stimulating factor (G-CSF) would be incorporated into the regimen. Due to platelet toxicity at the first dose level, T was changed to a 3-day regimen.

Results: 29 patients enrolled, 27 Stage III, and 2 Stage IV. Ages were 41 to 74 (median 56). A total of 85 cycles were given with the 3-day T. Delays occurred in 33 (39%), but were >7 days in only 11 (13%). 6 cycles were dose reduced. Grade 4 granulocytopenia occurred in 33 cycles (39%), but only 2 cycles (2.3%) were associated with febrile neutropenia. Platelets were <25,000 in 20 cycles (24%), but ≤10,000 in only 7 (8.2%), platelet transfusions were required in 3 cycles.

Conclusions: Myelosuppression is frequent but manageable with T and C. The MTD has not been reached at 1.0 mg/m^2/day. Cummulative toxicity in later cycles will probably prohibit further significant escalation of T.

934 POSTER

Positive progesterone receptor [PR+] and negative estrogen receptor [ER−] expression is associated with improved long term survival in ovarian cancer

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Purpose: Estrogen, progesterone as well as their receptors seem to be involved in the tumorigenesis in ovarian cancer. Their prognostic role is controversial.

Methods: Clinical, histological prognostic factors and steroid receptor status using semiquantitative immunohistochemistry (APAAP-method) were obtained retrospectively from 190 patients' records and stored formalin-fixed, paraffinembedded tumor tissue. Antibodies used: ER (clone 1D5) and PR (polyclonal) both DAKO Hamburg, Germany).

Results: Kaplan-Meier analysis revealed a significant influence of progesterone receptor expression ($P_{Log\ Rank}$ = 0.009) on survival and no influence of estrogen receptor expression. Both steroid receptors were coexpressed (ER+PR+) in 32.6%. ER+PR− tumors were found in 30.0%, ER−PR− tumors in 27.4%, and ER−PR+ in 10.0%. ER−PR+ tumors show a distinct better long-term survival if compared to the other steroid receptor combinations (mean survival 12.9 years; $P_{Log\ Rank}$ = 0.009). Correlation analysis reveals favorable associations between ER−PR+ receptor status and FIGO stage (P_{chi^2} = 0.039) as well as the volume of ascites at the time of primary surgery (P_{chi^2} = 0.069).

Conclusion: The reasons why ER−PR+ ovarian carcinomas are associated with favorable outcome, remain unclear, however, endocrine autoregulative processes, lack of susceptibility to unfavorable influences of estrogen and influences of progesterone, inducing cell differentiation and apoptosis may explain this effect.

935 POSTER

DICEP high dose (HD-DICEP) chemotherapy (CT) with or without peripheral blood stem cell support as consolidation treatment of patients (pts) with advanced epithelial ovarian cancer (AOC)

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Purpose: To analyse the impact and feasibility of consolidation treatment with HD-DICEP on disease-free survival (DFS) and overall survival (OS) in high risk AOC pts.

Patients and Methods: AOC pts (35) entered the study between 1992–1998. All patients were chemosensitive (platinum-CT, +/−taxol) and had low tumor burden at consolidation (determined by surgery in 29/35 pts). High-dose DICEP Seattle-protocol (Proc. ASCO 1993; 12: 50A) was applied. Median PS, 90 (80–100). Median age, 53 years (21–64). FIGO stages: IIIB, 2 pts; IIIC, 18 pts; IV, 6 pts. recurrent disease: 9 pts. Histologic subtype: Serous (S): 13 pts; endometrial (E): 10 pts; undifferentiated (U): 7 pts; mucinous (M) 2 pts; clear cell (C): 1 pts; unclassified (UN): 2 pts. Histologic grade (G): G-III, 22 pts; G-II, 4 pts; G-I, 1 pts; unknown, 8 pts.

Results: With a median follow-up of 51 months (4–75 m), median DFS is 12.5 months (3–68 m+), (median OS not reached). Most pts completed the treatment protocol (62 cycles-cy-/35 pts). 10 pts are long-time disease-free survivors: 2 pts had stage IV-liver parenchymal metastasis (UN: 38 m, and U-GIII: 42 m), 2 pts had recurrences (S-GII: 48 m, S-GIII: 24 m), 5 pts were