invasion, motility and attachment assays were performed in an in vitro assay system, 2) bikunin and uPA expression at the gene and protein levels were evaluated and 3) the animal model of the peritoneal carcinomatosis were made. The tumor weights and the ascites on 9th day after inoculation and the survival were evaluated.

Results: Bikunin gene transfection of HRA gave the following results: (1) transfection of HRA with the bikunin cDNA resulted in five variants stably expressing functional bikunin, as detected by ELISA, Western blot and immunohistochemistry; (2) bikunin transfectants produced significantly less uPA activity at the cell surface and the condition medium; (3) significantly reduced invasion, but not proliferation, adhesion, or migration relative to the parental cells and luciferase transfectants; and (4) animals inoculated with bikunin transfectants induced reduced peritoneal dissemination, tumor weights, tumoral ascites, invasion histologically and long term survival.

Conclusion: The present results suggest that transfection with bikunin gene induces suppression of tumor cell invasion, peritoneal dissemination and prolongs survival. This report shows that the predominant effect of transgenic bikunin overexpression by ovarian cancer cells is to inhibit their malignant phenotype.This pre-clinical animal model offers the possibility to explore gene therapy as a new treatment.

1193 POSTER

Molecular and molecular-cytogenetic analysis of y - chromosomal sequences from lymphocytes, undifferentiated gonads, disgerminomal and gonadoblastomal tissues in the patients with turner's syndrome (TS)

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Purpose: The presence of Y - chromosomal sequences, particularly gonadoblastoma locus GBY, in the patients with TS is a great risk factor for the development of gonadal tumour. The analysis is important both for prevention of gonadal tumours and for understanding of function GBY in carcinogenesis.

Methods: DNA isolated from 124 patients was amplified by polymerase chain reaction (PCR) and quantitative fluorescent PCR (QF PCR) in 4 loci. Y-positive cases were furthermore tested using fluorescent in situ hybridisation (FISH). The same techniques were used for the detection of Y- sequences in physiological and pathological tissues.

Results: Detection of Y sequences is described in the table (data in the table represent the ratio between the number of examinations and the number of positivities):

Technique	Locus					
	DYZ 3	AMGX/Y	SRY	PABX/Y	CEPY	PAINTY
PCR	124/6	124/4	102/4	50/2	X	X
QF PCR	124/17	124/7	X	X	X	X
FISH	X	X	X	X	18/3	7/3

Conclusion: The majority of hidden mosaicism is not detectable by conventional cytogenetic methods. QF PCR is the most sensitive and the most precise method for the assessment of Y chromosome mosaicism in patients with Turner syndrome. It enables the most effective selection of persons under the risk of gonadoblastoma development.

1194 POSTER

Magnetic resonance evaluation of pelvic teratomas

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Introduction: Magnetic Resonance Imaging (MRI) is an imagiological technique with high accuracy on the diagnosis of pelvic tumors.

Aim: To evaluate the ability of MRI on the characterization of pelvic Teratomas.

Material and Methods: We retrieved 16 cases with preoperative MRI exams and with the pathologic diagnosis of pelvic Teratomas, between July 98 and Mars 01. The mean age of patients was 44-years-old ranging from 25 ± 72 years, being 6 patients in the menopause. Eight tumors were located in the right ovary, 6 in the left ovary (one patient had a bilateral lesion) and two lesions were in the sacrococcygeal region. Tumor size range from 2 to 20 cm (mean: 8.3 cm). MRI images were obtained using a 1.0-Tesla superconducting magnet (model Gyroscan NT; Philips), and all exams included Gd-DTPA-enhanced fat-saturated T1-weighted images. The criteria used to classify the pelvic lesions as Teratomas by MRI was the presence of signal intensity similar to that of subcutaneous fat on T1- and T2-weighted images and that was suppressed by the fat-saturation sequence; and to classified the lesions as benign or malignant were the following criteria (significant solid component, septa thickness >3mm; vegetations; ascites; peritoneal/omental and/or pelvic organ involvement; adenomegaly).

Results: MRI identified all lesions but one as Teratomas. In 15 cases signal intensity similar to that of fat on T1- and T2-weighted images was found. In the misclassified case signal intensity similar to subcutaneous fat was not present in the T1 images and the purposed diagnosis was endometriosis. Fourteen cases were classified as benign and two as malignant lesions by MRI. All benign Teratomas were located in the ovary and the malignant tumors were in the sacrococcygeal region (one case had a solid vegetation and the other a thick septa). The histopathologic diagnosis confirmed the malignant transformation of sacrococcygeal region Teratomas.

Conclusions: 1 MRI is an accurate imaging technique on the characterization of pelvic masses containing fat.

2 MRI is able to detect malignant transformation in pelvic Teratomas.

1195 POSTER

Power Doppler with use of contrast in the differentiation of ovarian tumors

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Objetive: To differentiate benign ovarian tumors from malign ones before surgery, through the color and pulsed Doppler and to compare the obtained results before and after the use of contrast, thereby verifying whether there is an improvement of the diagnostic sensibility with its use.

Materials and Methods: 62 women were studied (age mean of 49.9 years) with ovarian tumors, 45 benign and 17 malign, and all of them were submitted to a transvaginal color Doppler ultrasonographic exam. A research of the arterial vascular flow was made in all tumor areas, as well as an impedance evaluation of same through the RI.

Results: The localization of the vessels in the tumor revealed a greater proportion of malign tumors with internal vascular flows (64%) than benign tumors with such flows (22%). There was a considerable overlap of these findings. The use of contrast identified a greater number of vessels with confirmation in the totality of tumors, but did not improve the Doppler capacity in tumoral differentiation. The malign tumors presented lower values of RI than the benign ones independently of the use or not of the contrast. The cutoff value for RI that better maximized the Doppler sensibility and specificity was 0.55. Through this value it was obtained an increase of the sensibility after the contrast use, varying from 47% to 82%, while the specificity maintained itself statistically equivalent.

Conclusion: The contrast use constitutes a promising advance aiming to differentiate ovarian tumors. Significant benefits can be expected particularly in patients with sub-optimal results by the ultrasonographic conventional Doppler exam.

1196 POSTER

Efficacy of paclitaxel in combination with intraperitoneal cisplatinum in patients with advanced ovarian cancer

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Aim: In this study, we investigated the efficacy and toxicity profile of intravenous paclitaxel used in combination with intraperitoneal cisplatinum in patients with advanced ovarian cancer.

Patients and Method: Twenty-six patients (pts.) who underwent optimal surgical cytoreduction at initial diagnosis (12 pts.;46.2%) or with persistent disease after first line chemotherapy following primary debulking surgery (14 pts.; 53.8%) were included in this study. Median age was 48 years (range: 27-62). At initial admission extent of disease was assessed as FIGO stage III-A: 6 pts. (23.1%), III-B: 2 pts. (7.7%), III-C: 13 pts. (50%), IV: 5 pts. (19.2%). Twenty three patients had residual tumors measuring 1 cm. or less.All patients were given intravenous paclitaxel at 135 mg/m2 as a 3 hour infusion and cisplatinum at 75 mg/m2 intraperitoneally on

the first day with 3 weekly intervals. Patients without a definite clinical or radiological evidence of disease progression underwent surgical laparotomy for response assessment.

Results: Pathologic complete response was attained in 19 pts. (73.1%). One patient (3.8%) had progressive disease. After a median follow-up period of 29 months (10-64), 13 pts. (50%) are alive with no evidence of disease, 4 pts. (15.4%) are living with their underlying disease and 9 pts. (34.6%) have died due to tumor progression. Median response duration in those with primary and persistent disease are 17 months (0-48) and 12 months (0-40), respectively. Out of 205 cycles, WHO grade III and IV toxicities were documented as follows: anemia 3 pts (11.5%), neutropenia 2 pts. (7.7%), thrombocytopenia 2 pts. (7.7%), emesis 6 pts. (23.1%), renal toxicity 3 pts. (11.5), diaarhoae 1 pt. (3.8) and alopecia 17 pts (65.4%). A neutropenic febrile episode was observed in 1 patient. Intraperitoneal treatment caused grade III abdominal pain in 3 patients.Three pts. (11.5%) had catheter-related complications; which necessitated an alteration to intravenous (IV) cisplatin treatment in 2 pts. In 3 pts. intraperitoneal cisplatin had to be replaced by IV carboplatinum due to severe nephrotoxicity. There were 4 cycles of treatment delays due to hematologic toxicity in 2 pts., nephrotoxicity and severe emesis in 1pt. and an autitis episode in 1 pt.

Conclusion: Intraperitoneal cisplatinum combined with IV paclitaxel at 135 mg/m2 as a 3 hour infusion is an effective and safe combination for the treatment of advanced ovarian cancer.

1197 POSTER

Independent prognostic factors who predicted progressive disease in advanced ovarian cancer

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This study was undertaken to assess the prognostic value of thirteen variables in 222 patients with advanced ovarian cancer related to the interval to progression.

Besides the pretreatment CA125 values, marker kinetiks and CA125 half-life (T1/2), ten other common clinicopathological variables were investigated: age, type of surgery, disease stage, Karnofsky index, residual disease, histological type, histological grade, type of cisplatin chemotherapy (PAC, PC, PA), number of chemotherapy cycles (CT) and treatment response.

Serial determination of tumor marker CA125 were performed in all patients. T1/2 was calculated in 122/222 patients, according to the van der Burg's formula. CA125 kinetics could be estimated only for patients whose prechemotherapy levels were above 35 U/ml, i.e. 134/222 patients.

A univariate analysis (log-rank, Tarone-Ware, Breslow and univariate Cox analysis) estimates the effect of each prognostic factor individually, not taking into consideration coexisting prognostic factors. Statistical significance was observed for the following out of 13 investigated variables: age, type of surgery, FIGO stage, histological grade, residual disease, Karnofsky index, number of chemotherapy, CA125 kinetics and C A125 half-life (T1/2). A multiple regression analysis based on Cox's proportional hasard model was used to test the relative importance of variables as predictors of free interval to progression. The indipendent predictors in order of significance are: Karnofsky index ($p<0.0001$), T1/2 ($p=0.0011$), CA125 kinetics ($p=0.0014$), histological grade ($p=0.0087$) and residual disease ($p=0.0191$).

As consequence, the possibility to predict treatment response by the CA125 half-life during CT and the time need for normalization of CA125 levels can divide patients into good and poor prognostic group early during CT.

1198 POSTER

Are p27,p21 and p53 prognostic factors in ovarian carcinoma patients?

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p21, p27 and p53 have been shown to be of prognostic significance in different human tumors.

Material and methods: Using immunohistochemistry, we examined p27, p21 and p53 in a series of 76 consecutive SEN (Serous Epithelial Neoplasia) pts. Thirteen borderline tumors were excluded from this analysis, leaving 53 primary ovarian (31 serous papillary, 22 other histotypes) and 10 serous surface papillary carcinomas, with a median follow-up of 38 months (range: 2-84).The carcinomas were graded according to WHO (3 G1, 33 G2, 19 G3 and 8 G4) and staged according to the FIGO criteria (24 S I-II and 39 S III-IV).Immunostaining monoclonal antibodies were K2502 (p27), EA10 (p21) and DO7 (p53).Cases were considered positive if the percentage of stained tumor cells was above the median value of 20% for p27 and p53, and 2.5% for p21.

Results: Among the 63 evaluable tumors, 55.5% showed a clear p53 overexpression and 49.2% showed low p27 and p21 expression.

No relation was seen neither between p53 and p21 nor between p27 and p21.

No significant relation was also observed between these markers and tumor histotype, grade or stage, although a trend was seen for higher grade tumors to overexpress p53.DFS and OS appeared to be correlated with grade ($p=0.02$ and $p=0.01$), stage ($p<0.0001$ and $p=0.004$) and p53 expression ($p=0.03$ and $p=0.02$), but not with the combined p53/p21 phenotype.At 4 years, DFS and OS were statistically worse (30% and 56%) in p53 positive tumors than in p53 negative (61% and 75%).

Conclusions: these data appear to confirm the worse prognosis of p53 overexpressing ovarian cancers, while p21 and p27 don't seem to correlate with clinical outcome.

1199 POSTER

A phase II trial of a paclitaxel and oxaliplatin combination in advanced ovarian cancer patients pretreated with cisplatin or carboplatin ± taxanes: Preliminary results

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Purpose: The aim of this ongoing study is to evaluate the efficacy and safety of a paclitaxel and oxaliplatin combination in patients with advanced ovarian cancer (AOC) and clinically measurable disease, pretreated with one platinum based regimen ± taxanes, with a platinum-free interval of at least 6 months.

Patients and Methods: As of March 2001, the first 24 patients (pts) entered in 9 French centers had been externally reviewed. Median age was 61 years (40–76), and performance status was 0 = 12 pts, 1 = 9 pts, 2 = 3 pts. Platinum free interval (PFI) was >12 months in 16 pts, and 6–12 months in 8 pts. Paclitaxel 175 mg/m^2 was administered over 3 h followed by oxaliplatin 130 mg/m^2 over 2 h every 21 days for a maximum of 6 to 9 treatment cycles.

Results: Twenty-two pts (115 cycles) were eligible and evaluable for efficacy and toxicity, 14 of whom were taxane-pretreated. An ORR of 91% was achieved with CR observed in 5 pts, PR in 15, and SD in 2. Median follow up was 7 months (4–16); 6 pts progressed (at 7, 7, 8, 10, 11, and 12 months), and no deaths occurred. The median number of cycles received was five (2$^+$–9). Grade 3 and grade 4 neutropenia occurred in 33% and 13% of cycles, respectively, with a single episode of febrile neutropenia. Grade 3 thrombocytopenia was observed in 1% of cycles, grade 3/4 nausea and vomiting in 3%, grade 3 asthenia in 4%, and grade 3 allergic reaction in 2%. Reversible neurotoxicity ≥ grade 2 (NCI-CTC) was observed in 54% of pts after a median of 4 cycles (3–6) and led to treatment discontinuation after six cycles for one patient.

	Prior taxanes	N = 14	No prior taxanes N = 8		Total (N = 22)
PFI (months)	6–12	>12	6–12	>12	-
CR + PR (pts)	6	7	1	6	20 (91%)
SD (pts)	1	–	–	1	2 (9%)

Conclusion: These encouraging results indicate that the paclitaxel and oxaliplatin combination is safe and very active in platinum-pretreated AOC patients with a platinum-free interval of at least 6 months.

1200 POSTER

Relapsed ovarian cancer after failure of first-line chemotherapy with platin and paclitaxel -a phase II study

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Background: Topotecan (T), a topoisomerase I- inhibitor, is approved for