

Mean age was 56 years. Stage IIIA 3pts, IIIB 15pts, IIIC 45 pts, IV 5 pts. There was one toxic death (2%). With a median follow-up of the study of 8.25 years, median overall survival is 75 months and median progression-free survival is 41 months. At 5 years, 60% are alive and 32% didn't relapse. Intensive consolidation IP CT after negative SLL can improve survival in AOC. However, due to late relapses the cure rate remains disappointingly low, even in this most favorable patients category. Long-term follow-up (more than 5 years) is therefore needed to further evaluate strategic treatment options.

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POSTER

Cisplatin nephrotoxicity

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Introduction: Cisplatin (CP) is an antineoplastic agent active against ovarian tumours but nephrotoxicity is often dose-limiting.

Objective: To determine the incidence of acute and chronic nephrotoxicity of CP, the risk factors associated with its development and the influence of two different types of prophylactic hydration.

Materials and methods: We have retrospectively studied 132 patients who received CP in the treatment of ovarian cancer in the Portuguese Institute of Oncology Francisco Gentil between 1995 and 2000. They all had a normal plasma creatinine concentration before treatment. They received a dose per course of 75 mg/m², with a minimum of 6 courses and a maximum of 12 courses of chemotherapy (CT). There were 2 different courses of prophylactic hydration: 'prolonged hydration' (4000cc of saline in 20 hours) and 'short hydration' (3000cc of saline in 6 hours). Acute Renal Failure (ARF) was defined as a doubling in the plasma creatinine concentration and isolated Tubulopathy (IT) as the appearance of hypomagnesaemia without a concomitant rise in plasma creatinine concentration. Chronic Toxicity (CT) was defined as a doubling in the plasma creatinine concentration, 6 months after chemotherapy.

Results: There was evidence of nephrotoxicity in 78 patients (59%); 53 (40%) had ARF and 25 (19%) IT. Most toxicity developed after the 6th course of CT with an average cumulative dose of 720 mg. Age was significantly associated with nephrotoxicity (58.1 ± 11.8 vs 49.3 ± 14.1 ; $p < 0.0001$), dose of CP per cycle (118 ± 17 vs 104 ± 30 ; $p < 0.005$), and highest cumulative dose (797 ± 254 vs 680 ± 221 ; $p < 0.01$). In 12 patients CT was suspended due to side effects. 20 patients died during treatment. There was no significant statistical difference between the two types of prophylactic hydration. CT was seen in 29 patients (22%) and was significantly associated with age (59.5 ± 13.6 vs 53 ± 13.1 ; $p < 0.05$).

Conclusion: Acute nephrotoxicity of CP has a high incidence. Age, dose of CP per course of CT and cumulative dose of CP, are risk factors for toxicity. There were no differences in the incidence of nephrotoxicity between the two prophylactic courses of hydration. Development of chronic nephrotoxicity is frequently related with the age.

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POSTER

The predictive value of computerized tomography (CT) for surgical findings in ovarian cancer patients

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Objective: Pelvic and abdominal computed tomography (CT) is usually performed in patients (pts) with ovarian cancer (OC) to evaluate the diseases extent as well as the response to therapy. The purpose of this retrospective study was to evaluate the role of CT scan in predicting pathologic response to systemic chemotherapy, in pts with OC.

Methods: We retrospectively reviewed the abdominopelvic CT scans performed after the completion of three or more cycles of Platinum based chemotherapy in 29 pts with proven epithelial ovarian cancer and residual lesions after primary surgery. These CT findings were compared with subsequent laparotomic findings.

Results: The correlation between radiologic and laparotomic findings was concordant in 72% (21/29) of pts and discordant in 27% (8/29).

After chemotherapy, 14 CT were negative (Clinical Complete Remission) and 15 were positive (14 Remission Partial and 1 Stable Disease), but between the 14 pts with negative CT there were only six pathological Complete Remissions whereas all 15 pts with positive CT were positive at surgery. Cumulatively laparotomy revealed either microscopic or macroscopic residual lesions in 23 pts, while 6 pts were completely tumour-free.

Conclusions: In our experience a positive CT always corresponded to positive surgical findings whereas a negative CT correlated with pathological Complete Remission only in 42% of the cases.

The positive predictive value was 100% and the negative predictive value of CT was only 38.4%.

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POSTER

Recurrent granulosa cell tumor of the ovary: Retrospective analysis

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Purpose: In this study, patients with Granulosa cell tumours (GCT) were evaluated retrospectively and recurrent cases characteristics and treatment outcomes were documented.

Methods: Forty-five patients (4.7%) with GCT were treated among 952 patients with ovarian cancer between 1979-1998. Nine of 45 patients (20%) developed recurrent disease on follow-up. All patients but one (stage Ia) had stage III disease. The specific recurrence sites were intraabdominal (liver, peritonea, spleen), 4; pelvic, 2; pelvic+intraabdominal, 2; lung, 1. Patients with only pelvic recurrence received only pelvic radiotherapy (2 patients) and patients with distant (intraabdominal, lung) ± pelvic recurrence received only chemotherapy of cisplatin, doxorubicine, cyclophosphamide (PAC) or cisplatin, cyclophosphamide (PC) (5 patients). The other two patients with intraabdominal recurrence refused to receive treatment.

Results: The median age was 46 (16-54) years. The median recurrence time was 19 (5-29) months. Patients with only pelvic recurrence receiving only radiotherapy were dead of their disease progression 5 and 6 months from the diagnosis of recurrence. The other two patients who had no treatment were also dead of their disease progression 11 and 13 months after the recurrence. Among patients received chemotherapy, three complete and 1 partial responses were observed, for an overall response rate of 80%. One patient had progressive disease under the chemotherapy. Three of 5 patients received chemotherapy were dead of their disease progression 26, 41, 52 months while two patients who had complete response were alive without evidence of disease 25 and 33 months from the diagnosis of recurrence. The median survival after recurrence for all patients was 21 (5-52) months.

Conclusion: Despite the small number of patients in our study it can be concluded that chemotherapy may be the treatment of choice for recurrent granulosa cell tumour of the ovary.

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POSTER

Suppression of invasion and peritoneal carcinomatosis of ovarian cancer cell line by overexpression of bikunin

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Purpose: Bikunin, a Kunitz-type proteases inhibitor, was isolated from human amniotic fluid and urine. We previously reported that bikunin efficiently inhibits soluble and tumor cell-surface receptor-bound plasmin. Bikunin inhibits not only tumor cell invasion in an in vitro assay but also production of experimental and spontaneous lung metastasis in an in vivo mouse model. Recently, we reported that bikunin markedly suppresses the cell motility possibly through negative regulation of PKC- and MEK/ERK/c-Jun dependent uPA expression.

In this study we first transfected an expression vector harboring a cDNA encoding for human bikunin to human ovarian carcinoma cell line HRA, highly invasive cells, and investigated the effect of bikunin overexpression on the changes in tumor cell phenotype and invasiveness in the stably transfected clones.

Methods: We made bikunin transfectants and luciferase transfectants as a control vector. The parental cells were used as control. 1) Proliferation,

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.

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POSTER

Molecular and molecular-cytogenetic analysis of Y-chromosomal sequences from lymphocytes, undifferentiated gonads, disgerminal and gonadoblastoma 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	AMG/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.

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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.

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POSTER

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

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Objetive: To differentiate benign ovarian tumors from malignant 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 malignant, 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 malignant 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 malignant 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.

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POSTER

Efficacy of paclitaxel in combination with intraperitoneal cisplatin 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 cisplatin 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 cisplatin at 75 mg/m² intraperitoneally on