

84.6% for both cases and controls (RR 1.00, CI 0.35–2.83). The size of the group with advanced carcinoma was too small to allow any statistical analysis. The moment at which the diagnosis was made (trimester of pregnancy or post-partum period) and mode of delivery (abdominally vs. vaginally) had no impact on survival. No differences were observed in the prevalence and type of early and late complications of standard oncological therapy (surgery and/or radiotherapy). **Conclusion:** The prognosis of early stage CC is similar in gestational and non-gestational patients, provided standard oncological therapy is given. Due to the limited number of patients no conclusions can be drawn about advanced stage of CC. Standard therapy does not lead to increased morbidity in gestational patients and should be aimed for.

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ORAL

SIGNAL CHARACTERISTICS ON HIGH RESOLUTION MRI MAY PREDICT OUTCOME AMONG PATIENTS WITH BULKY CERVIX CANCER TREATED BY IRRADIATION

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Background: We have previously reported the ability of high resolution (400 × 400 μ M) T2 MRI scanning with the endorectal coil (eMRI) to evaluate the extent of disease and predict initial response to radiotherapy (RT) in patients with cancer of the uterine cervix. The current report provides long-term follow-up on a cohort of 14 patients. **Methods:** 14 women with bulky (>6 cm) cervix cancer (stages Ib–IVa) were evaluated prior to definitive RT (median point A dose 85 Gy) with eMRI. Signal intensity was graded as bright, intermediate, or low. Patients were followed at 6 month intervals. **Results:** Three patients with bright signal intensity have been maintained without evidence of recurrence at 44, 47, and 48 months, respectively. The remaining woman with bright signal died of disseminated disease (brain mets) but remained without local progression at the time of death (31 months). The 3 patients with low signal intensity never derived local control and quickly succumbed to their disease (5, 15, and 18 months). Of the 7 patients with intermediate signal intensity, one is free of disease at 21 months, one responded partially and was salvaged by adjuvant hysterectomy to be NED at 38 months, 5 responded partially and died of local progression. The sample size did not justify multivariate analysis to rule out interaction with other discriminants of outcome (stage, total RT dose, overall Tx time). **Conclusions:** With prolonged follow-up, bright signal intensity on eMRI is prognostic of freedom from local relapse and low signal intensity is associated with rapid cancer death. Possible underlying mechanisms will be presented. Other groups are encouraged to confirm these findings among larger samples of patients with bulky tumors.

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ORAL

EFFECT OF TOTAL TREATMENT TIME ON PROGRESSION-FREE AND OVERALL SURVIVAL IN CERVIX CARCINOMA

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In order to determine the effect of radiation therapy duration in cervix carcinoma, 458 patients with FIGO stage IB–IIIB were retrospectively analysed. They were classified according to whether they had rather long therapies, taking 60 days (the 75th percentile) as an arbitrary cut-off. Median therapy duration was 44 days. The 5-year progression-free survival and the 5-year overall survival were respectively $61 \pm 3\%$ and $64 \pm 3\%$ for the less than 60 days group, and $39 \pm 6\%$ and $47 \pm 6\%$ for the more than 60 days group ($p < 0.001$). In terms of univariate hazard ratio (HR), the relative difference between the two groups corresponds to an increase in hazard of local recurrence, distant metastasis and death of the double (HR = 2.09, 95% CI [1.51–2.89]) ($p < 0.001$). A multivariate analysis, including selected prognostic factors, confirms these results (HR = 2.01, 95% CI [1.35–2.99]) ($p < 0.001$). In terms of overall survival the relative difference between the long and the short therapy duration was of the same order as for progression-free survival.

In conclusion a short treatment time duration is a highly significant prognostic factor, associated with longer progression-free and overall survival in cervix carcinoma.

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ORAL

p53 PROTEIN AS A PREDICTOR OF SURVIVAL IN ENDOMETRIAL CARCINOMAS

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In an immunohistochemical study tumor specimens from 183 women with endometrial carcinoma were analysed as regards p53 expression, using the monoclonal antibody DO-7. Negative specimens were 101 (55%), whereas the staining intensity was weak, moderate or strong in 27 (15%), 4 (2%) and 51 (28%), respectively. DNA content was analysed in 159 (87%) tumors. Moderate or strong expression of p53 were significantly more common in aneuploid tumors ($P < 0.0001$). S-phase fraction was evaluable in 165 cases. High S-phase fractions were more frequent in with strong expression of p53 ($P < 0.0001$). p53 expression was correlated to grade ($P < 0.05$) but not to clinical stage. In histological subgroups such as UPSC (Uterine Papillary Serous Carcinoma), clear cell carcinoma and undifferentiated carcinoma of the endometrium, strong expression of p53 was more frequent. Moderate or strong expression of p53 was highly predictive of a poor survival ($P < 0.001$).

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ORAL

THE IMPACT OF ADJUVANT RADIOTHERAPY ON MALIGNANT MIXED MULLERIAN TUMORS OF THE UTERUS

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Malignant mixed Mullerian tumors (MMMT) comprise less than 5% of uterine malignancies. The role of adjuvant radiotherapy (RT) for this rare tumor is unclear. We reviewed our experience with 64 uterine MMMT patients (49 FIGO stage I/II, 15 stage III). Thirty-one patients received adjuvant RT following definitive surgery (21 stage I/II, 9 stage III) and the remaining 33 were observed only (27 stage I/II, 6 stage III). Mean follow-up was 50 months. Local failure was found to be significantly reduced ($P < 0.001$) with the addition of RT. Local failure was 3% in the RT group compared with 48% in the unirradiated group with mean time to local failure of 8 months. No such difference was seen in the incidence of distant failure (33% versus 35%) with mean time to distant failure of 28 months in the treated group and 7 months in the untreated group. Mean time until death was 36 months for the treated group and 14 months for the untreated group. These results demonstrate that adjuvant radiotherapy plays an important role in achieving local control as well as improving length of progression-free survival in women with uterine MMMT.

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POSTER

THE RISK FOR MALIGNANT PROGRESSION OF VULVAR NON-NEOPLASTIC EPITHELIAL DISORDERS: A PROSPECTIVE STUDY

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Vulvar Lichen Sclerosis (LS) and Squamous Cell Hyperplasia (SCH), known as "vulvar non-neoplastic disorders", have a strong topographic association and co-existence with Squamous Cell Carcinoma of the vulva (SCCV). In the last 10 years, 156 patients (pts) with vulvar non-neoplastic epithelial disorders were referred to our Center. Eleven women were lost to follow-up and nine died of unrelated causes. Of the remaining 136 pts who were treated and followed, 14 (10.3%) progressed to SCCV. Of these 14, three had SCH, six had LS and five had mixed lesions. Three of these pts refused topical treatment and 11 did not respond to any topical preparation offered. All 14 were surgically treated and malignant recurrence was documented in nine (eight from the group that failed to respond to topical preparations and one from the group that refused topical treatment). This study suggests that pts who do not respond to conventional topical therapy should be regarded as being at high risk for malignant progression.

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POSTER

UTERINE SARCOMAS: PROGNOSTIC FACTORS AND TREATMENT MODALITIES

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From 1974 to 1992, 65 patients with uterine sarcomas were referred to Instituto Português de Oncologia—Porto. All patients were retrospectively staged according to accepted UICC criteria. The distribution

by histologic type was the following: Leiomyosarcoma (LMS)—33 patients (50.8%); mullerian mixed mesodermal tumor (MMM)—14 patients (21.5%); endometrial sarcoma (ES)—16 patients (24.6%) and other histologies—2 patients (3.1%). Overall survival at 2 and 5 years was 74% and 58%, respectively. Age at presentation, initial symptoms, parity and associated medical conditions were recorded. Overall survival (OS) and disease-free survival (DFS) were analysed by histologic type, hormonal status, tumor extension and treatment. Tumor extension and hormonal status were the most important factors in predicting survival ($P < 0.01$). No significant difference for prognosis was found for histologic type and medical associated conditions. All patients were treated with surgery (S), radiation therapy (RT), chemotherapy (CT) and hormonal therapy (HT), alone or combined. T1 e T2 patients which underwent postoperative RT did significantly better than those treated with S alone (77% vs 35% 5-year DFS; $p < 0.007$). The best results were obtained in the subgroup of patients treated with S + RT + CT (81% 5-year DFS). There was a significantly lower rate of pelvic recurrence among the women treated with RT ($P = 0.01$) and a slight tendency to a lower rate of distant failures among those treated with CT ($P = 0.07$).

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POSTER

PROGNOSTIC VALUE OF HISTOLOGICAL TUMOR REGRESSION AFTER IRRADIATION FOR UTERINE CERVIX CARCINOMA

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Radio-surgical combination is an effective treatment for centro pelvic cervix carcinoma. Using preoperative radiotherapy, 80% of the patients have no residual disease at the time of surgery. The purpose of this study was to determine the prognostic value of the cervix sterilization after initial irradiation.

Patients and methods: Between 1976 and 1993, 200 patients with histologically proven cervix carcinoma (91 patients with clinical stage Ib tumor, 91 with stage IIA, and 18 with stage IIB) have been treated by irradiation followed by radical hysterectomy 6 weeks later. The mean age was 48 years. Median follow up was 86 months. One hundred and five patients underwent an utero-vaginal application of caesium 137. A dose of 60 Gy was delivered in the reference volume followed by radical hysterectomy and lymphadenectomy. Ninety five patients with bulky centro pelvic tumors received an external pelvic irradiation, a brachytherapy and surgery. The mean dose to whole pelvis was 40 Gy (18–50).

Results: Uncorrected five-year overall survival rate was 96% for stage Ib, 61% for stage IIA and 48% for stage IIB.

Sterilization rate after irradiation was 82% for stage Ib, and 61% for stage IIA or IIB. Probability of survival was significantly better in case of tumor sterilization with a 5-year survival rate of 78% versus 65% and 61% for patients with microscopic residual disease and macroscopic persistent tumors, respectively. In univariate analysis, stage and node status according to the lymphography were prognostic factors. A multivariate analysis should be presented.

Conclusion: histological sterilization after irradiation appeared as a favorable prognostic factor.

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POSTER

A PHASE II STUDY OF CPT 11 (IRINOTECAN) IN CHEMOTHERAPY NAIVE PATIENTS WITH ADVANCED CANCER OF THE CERVIX UTERI (C.C.U.)

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Patients with advanced C.C.U. without prior therapy have been treated with the new DNA topoisomerase I inhibitor CPT 11 350 mg/m² q 3 w. Patients were stratified depending on whether all the target lesions were within a field of prior radiation therapy (group B) or not (group A).

Criteria of Inclusion: Age ≤ 75 ; WHO PS 0–2; ANC $> 2 \times 10^9$ platelets $> 100 \times 10^9$, creatinine $\leq 130 \mu\text{mol/l}$, bilirubin $\leq 1.25 \text{ N}$, Transaminases $\leq 2 \text{ N}$ (except in case of liver metastases), presence of at least one measurable lesion.

Characteristics: 42 patients have been enrolled to date (median age 48 (30–71); median number of involved organs: 1(1–3) with primary in 46%, lung in 22%, liver and bone in 8% of patients. 27 patients were in group A and 15 in group B.

Efficacy: (Preliminary Results) CR: 1, PR: 4, the five responses have been observed among the 21 evaluable patients of group A (24%).

Safety: The following WHO grade 3–4 toxicities have been reported (% of patients): neutropenia: 27%, (with febrile neutropenia and/or sepsis in 8%), delayed diarrhea: 33%, nausea/vomiting: 30%, alopecia: 32%. One toxic death occurred due to severe diarrhea, neutropenia and sepsis.

Conclusion: The most concerning toxicity is the combination of severe diarrhea and neutropenia. Since these two toxicities are probably favoured by abdominopelvic radiotherapy, a special attention should be paid to patients with extended fields. CPT 11 appears an effective drug in not pretreated C.C.U.

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POSTER

PROGNOSTIC FACTORS AND PATTERNS OF FAILURE IN STAGE I ENDOMETRIAL CARCINOMA TREATED WITH ADJUVANT RADIOTHERAPY

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Purpose: To evaluate the therapeutic outcome of patients with high-risk for recurrence, to describe patterns of failure as well as other important pretreatment and treatment factors which can influence to improve control and lengthen survival. **Methods:** From 1989 to 1990, 213 patients with endometrial carcinoma with high-risk attributes and disease confined to pelvis were prospectively treated with adjuvant pelvic radiation. The median age was 59.2 years. The FIGO/1988/stage distribution was as follows: Ib/G2–G3/ = 61, Ic/G1–G3/ = 83, IIA/G1–G3/ = 10, IIB/G1–G3/ = 14, IIIA/G1–G3/ = 6, unknown stage /G1–G3/ = 39. All patients were treated with combined /EBRT/ICBHT/radiotherapy. The treatment was tailored to the known prognostic factors: grade 1 and greater than 50% myometrial invasion, grade 2 and 3 with less (33%) or greater than 50% myometrial invasion and involvement of the isthmus/cervix. Results were analyzed for specific, and relapse-free survival. **Results:** Overall 5 year survival was 79%. Five-year specific survival/5 yrs/per stage was 86% in stage Ib, 79% in Ic, 82% in IIA, 72% in IIB and 43% in IIIA. FIGO substage in addition to depth by thirds ($\leq 2/3$ vs $> 2/3$ /grade/1 vs 2 or 3/ age ≤ 55 vs > 55) were predictive for 5 years in univariate analysis. 5-year specific survival decreased with increasing grade and substage from 89% for grade 2 and substage Ib to 70% for grade 3 and substage Ic. $p < 0.001$ / the cervix invasion was more often associated with grade 3 /56% vs 21%/ and deep myoinvasion /64% vs 30%/ than cases without cervix invasion. 5-year relapse-free survival was 78%; 22% relapse, of which 19% distant and 3% local relapse. Multivariate analysis of the above factors revealed FIGO stage in addition grade, age and depth by thirds to be independent predictors of outcome. **Conclusion:** Patients with high risk attributes demonstrated to have disease confined to the pelvis can achieve excellent local-free survival following adjuvant pelvic radiation. However, prospective randomized trials in the same subset of high risk patients, employing adjuvant cytotoxic chemotherapy, hormonal therapy and/or whole abdominal-pelvic radiation should be considered in an attempt to improve survival.

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POSTER

A PHASE II STUDY OF GEMCITABINE IN ADVANCED CERVIX CARCINOMA

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In a phase II study in patients with locally advanced (Stage IIIB) and metastatic (Stage IV) histologically proven cervix carcinoma, gemcitabine was given at a dose of 1250 mg/m² weekly for 3 weeks (days 1, 8 and 15 followed by 1 week of rest), these 4 weeks constituting 1 cycle of chemotherapy. The patients were chemonaive, had adequate bone marrow reserves, liver and kidney function and bi-dimensionally measurable disease, pelvic disease being measured by means of magnetic resonance imaging. To date, 42 patients have been entered into the study and the data for the first 30 patients is available for analysis. Of these 30 patients, 28 are evaluable for efficacy analysis, having received at least 3 doses of gemcitabine within the first 7 weeks of study participation. 2 patients were not evaluable for efficacy because they did not receive 3 doses of gemcitabine. The average age of the patients was 50 years (29–64 years) and the proportion of stage IIIB and stage IV disease was 53% and 47%, respectively. A partial response has been confirmed in 5 patients giving a response rate of 17.9% (5/28). All 30 patients were evaluated for toxicity. The respective WHO grade 3 and 4 toxicities were: leukopenia 10%