1166 PUBLICATION

PROSPECTIVE TRIAL OF CHEMOTHERAPY AND RADIOTHERAPY FOR INVASIVE BLADDER CARCINOMA: PRELIMINARY RESULTS

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Purpose: This study was designed to improve local control and survival rates and to evaluate the possibility and safety of conservative treatment in invasive bladder cancer.

Material and methods: Between June-89 and March-94, 30 patients with invasive bladder cancer T2–4 Nx Mo, were entered prospectively on a selective bladder-sparing protocol combining aggressive transurethral resection (TUR), CMV chemotherapy and radiotherapy (60 Gy). Radical cystectomy was recommended to patients with residual disease after TUR-CMV. Eight non responders patients who refused surgery were given 66 Gy radiotherapy.

Results: Among the 90 evaluable patients, 24 (80%) are alive and free of disease (median follow-up of 32 months) and 22 (74%) have functional bladders. Radical cystectomy was performed only in 3 patients. Of the 27 patients who completed full-course chemoradiotherapy, 22 (81.5%) are alive and free of disease at the present time (included 3 who developed ca *in situ* and were treated successfully with intra vesical therapy). Several prognosis factors, including tumor stage and response to TUR-CMV, were found to be significant predictors of overall survival and distant metastases rate.

Conclusions: These results confirm that TUR, CMV and radiotherapy may be effective to improve cure rate maintaining a functional bladder.

Other gynaecological tumours

1167 ORAL

DEFINITIVE RADIOTHERAPY FOR CARCINOMA OF THE VAGINA—A LONG-TERM FOLLOW-UP STUDY

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Between 1953 and 1991, 301 patients with carcinoma of the vagina—271 with squamous cell (SCC), and 30 with non-clear cell adenocarcinoma—received definitive radiotherapy (XRT). Stages according to the FIGO system were: 0 37 (12%); I 65 (22%); II 122 (40%); III 60 (20%); and, IV 17 (6%). Treatment varied according to stage, location and presence or absence of uterus. Although adenocarcinoma accounted for a small proportion of cases, it's outcome was significantly worse for all endpoints than for SCC and remained worse; the remaining abstract refers solely to SCC. The patterns of failure were as follows: local 69 (23%); pelvic nodal 21 (7%); inguinal nodal 12 (4%); distant metastatic 39 (13%); and, any relapse 106 (35%). All inguinal node failures occurred in patients with lesions of the lower vaginal third. The major independent determinants of metastases were FIGO stage, tumor bulk, and local recurrence. Treatment technique did not correlate with outcome. Survival at 5, 10 15, 20, and 25 years was 62%, 52%, 40%, 30%, and 24%, respectively. Significant treatment-related complications occurred in 42 women (14%).

1168 ORAL

ETOPOSIDE AND ACTINOMYCIN D (EA) FOR METHOTREXATE (MTX) RESISTANT, LOW RISK, PERSISTENT GESTATIONAL TROPHOBLASTIC DISEASE (GTD) AND EA WITH MTX (MEA) FOR HIGH RISK GTD

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Between 1986 and 1994, 174 patients were treated for persistent GTD. 146 received low dose MTX, of whom 113 were cured. 27/146 (18.5%) did not achieve normal HCG levels and received EA as salvage treatment (Etoposide 100 mg/m^2 and Actinomycin D 0.5 mg daily for 3 days, 7 day interval *et seq*), 26/27 (96.3%) were cured with thin regimen and 1 required subsequent MEA (see below) before being cured.

6/146 relapsed between 2 and 40 months after complete remission. 1 was cured with EA, 4 with MEA and 1 requires ongoing salvage therapy.

21 patients received primary MEA (MTX 100 mg/m^2 over 1 hour followed by 200 mg/m^2 over 12 hours, 7 day break then EA as above, 7 day break (*et seq*) for high risk disease, of whom 14 (66.7%) were cured. 3 were only cured after salvage treatment. 4 older patients with unusual histology died despite attempts at salvage.

Toxicity with both EA and MEA was expected. There were no treatment related deaths or second tumours. All patients developed total alopecia. Myclotoxicity was common though not usually significant.

It is concluded that EA and MEA are novel, safe and effective therapies for the treatment of MTX resistant low risk and high risk GTD respectively.

1169 ORAL

PLACENTAL SITE TROPHOBLASTIC TUMOURS AT CHARING CROSS 1975–1995

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Placental site trophoblastic tumour (PSTT), is a very rare variant of gestational trophoblastic disease characterized as a tumour of non-villous. cytotrophoblastic cells. It differs from choriocarcinoma (CC) histologically and immunocytochemically. Serum hCG levels are a less sensitive and specific tumour marker in PSTT than CC.

Over the last 20 years, 18 patients with PSTT have been treated at the Charing Cross Trophoblastic Disease Unit. Nine patients had metastatic disease at presentation (5 pulmonary, 3 pelvic & 1 extensive). The mean serum hCG at presentation was 1861 iu/l (range 33–20710). One patient with localised disease declined hysterectomy and achieved a spontaneous remission and is currently pregnant a second time after her PSTT. Two patients went into remission after hysterectomy alone, the remainder received combined surgery and chemotherapy (2 in an adjuvant context). Fourteen patients (78%) are alive in remission. The mean follow-up is 5.3 years, the median survival has not yet been reached but the 5 year survival is 75%.

An interval of more than 2 years between the antecedent pregnancy ($P = 0.0013$) and age over 30 years ($P = 0.032$) were independent adverse prognostic factors in multivariate analysis.

The behaviour of PSTT is unpredictable. There appears to be a lower propensity to metastasise and more chemoresistance than choriocarcinoma. The optimum approach for localised disease is surgical with or without chemotherapy. The management of metastatic disease remains unsatisfactory.

1170 ORAL

THE PROGNOSIS OF CERVICAL CANCER ASSOCIATED WITH PREGNANCY

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To evaluate the influence of pregnancy on the course and survival of cervical cancer (CC) we performed a matched cohort study. 44 patients with gestational CC and treated with standard oncological therapy were matched to 44 contemporary controls. Matching criteria were age, FIGO stage, tumor type, treatment modality. *Results:* In 23 cases CC was diagnosed during pregnancy, in 21 cases within 6 months after delivery. 39 patients had an early stage of CC (8 IA, 25 IB, 6 IIA) and 5 had an advanced stage (4 IIB, 1 IIIB). For early stages the 5 year survival rate was

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.

1171 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 μM) 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.

1172 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 ± 3% and 64 ± 3% for the less than 60 days group, and 39 ± 6% and 47 ± 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.

1173 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 ($P < 0.001$).

1174 ORAL

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

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Malignant mixed Mullerien 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.

1175 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.

1176 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