End 05

ADJUVANT HORMONOTHERAPY (TAMOXIFEN VERSUS MEDROXYPROGESTERONE ACETATE VERSUS CONTROL) IN WOMEN WITH ENDOMETRIAL CANCER, FIGO STAGE I AND II

M. Kaufmann, K. Brunnert, R. Mösch, U. Stosiek, R. Stiglmayer, J. Müller and R. Kreienberg

In a randomized prospective controlled trial a hormonotherapy with tamoxifen (Nolvadex^{R}: 30 mg PO/d) is compared with medroxyprogesterone acetate (Farlutal^{R}: 500 mg PO/d), and with no adjuvant treatment in patients with stage I and II endometrial cancer. Endocrine treatment is given for two years.
In this preliminary review of the data 143 evaluable cases have been accrued since April 1983. Each of these patients with histologically confirmed invasive carcinoma underwent surgery (± intravaginal radiation) or surgery plus radiotherapy (50 Gy external radiotherapy to pelvis in 4-6 weeks in grade 3 carcinomas or more than one third myometrial invasion). Surgery for stage II patients was radical hysterectomy. Endocrine therapy is started within 2 weeks after primary treatment.
One-hundred and twenty-four patients were FIGO stage I and nineteen stage II. One-hundred and eighteen patients had surgery alone, and 25 patients surgery plus radiotherapy. Histologic grade 1 was seen in 63, grade 2 in 58, and grade 3 in 22 cases. In 74 out of 143 (=52%) patients progesterone receptors could be determined. Eighteen (=24%) patients were receptor negative (≤ 20 fmol/ml cytosolprotein; DCC-method).
Til now 43 patients received tamoxifen, 50 medroxyprogesterone-acetate, and 50 women had no further adjuvant therapy.
Side effects and recurrence rates will be presented for each prognostic subgroup (stage, histologic grade, myometrial invasion and steroid hormone receptors.

Univ.-Frauenkliniken Heidelberg, Mannheim, Mainz und Frauenkliniken Karlsruhe und Baden-Baden.

End 06

ACIDIC, TUMOR SPECIFIC, ISOELECTRIC VARIANTS OF HCG IN TROPHOBLASTIC DISEASES

K. Mann, C. Clemm, G. Staehler and W. Eiermann

The aim of this study was to characterize and purify tumor specific hCG variants from patients with trophoblastic diseases. Analytical and preparative isoelectric focusing (IEF) of serum and purified hCG fractions was done on polyacrylamide gels, which were sectioned into 5 mm slices, extracted with 1 ml PBS and radioimmunoassayed using anti-hCG-ß and anti-hCG antisera. For quantitative determination of acidic hCG variants in serum samples, gelslides pI 3.3-4.0 and 4.0-5.2 were pooled, eluted in 1 ml buffer and determined by RIA, in the supernatant of tumor tissue after homogenization and sonification. HCG was purified from ultrafiltrated urine of patients with testicular cancer by chromatography on DEAE-Trisacryl-M, SP-Trisacryl-M and Ultrogel AcA 44 and was finally separated by preparative IEF. The purity was proven by gradient SDS-electrophoresis (4-22%)+4% mercaptoethanol. The percentage of acidic variants pI 3.3-4.0 to total hCG pI (3.3-4.0/3.3-5.2)x100 (%) varied from 8-46% in sera of 17 untreated patients with testicular cancer, 5 with hydatidiform moles and 3 with choriocarcinoma, but only from 0-4% in sera of pregnant women. Comparison of tissue extracts and serum samples of patients with testicular cancer showed similar results (tissue 16%,14% vs. sera 21%,8%). Only the urine of patients with trophoblastic tumors contained acidic hCG variants, which were not detectable in significant amounts in the native urine nor in purified hCG preparations from pregnant women. In SDS-PAGE (+ß-ME) the apparent molecular weight (Map) of the ß-subunit of hCGav was slightly larger than that of hCG CR 119 (Map 35,470 vs. 32,530; n=4) whereas the α-subunits were similar (Map 22,230 vs. 21,380; n=4).
In conclusion, tumor specific, acidic isoelectric hCG variants exist. Their ß-subunit is larger than that of hCG from pregnancy.

Medizinische Klinik II, Klinikum Großhadern der Universität München, Marchioninistr. 15, D-8000 München 70

Ova 01

MORPHOMETRY OF OVARIAN CANCER - CORRELATION WITH PROGNOSIS

B. Miller, D.V. Horbelt, L.A. Lavia

Tumor grade has a great influence on prognosis in ovarian cancer. Size and shape of nucleus and nucleolus are an important index of tumor differentiation and objective measurement of these features would help standardize tumor grading. We looked at patients with epithelial ovarian cancer, stage III and IV, histological grading II and III, after treatment with tumor reductive surgery and mephalan. Three groups were formed: I. n=6, residual 2cm, mean survival time 9,1 months; II. n=4, residual 2cm, mean survival time 66 months; III. n=4, residual 2cm, mean survival time 125 months. Electronmicroscopical pictures were used for morphometrical analysis with the videoplan system by Zeiss.

	X nucl.area	st.dev	X nucleol.ar.	st.dev.
I.	44,4	29,7	2,8	2,0
II.	30,4	16,2	2,2	1,5
III.	29,2	15,2	1,9	1,2

Tumors of group I were found to have the largest nucleolar area per nucleus (1,7 versus 1,1 and 0,9) and more nucleoli per nucleus (mean 0,6 versus 0,4 and 0,5).
Tumors leading to poor clinical outcome were found to contain larger nuclei with a higher degree of variation as well as more and larger nucleoli. Differences regarding clinical outcome between group I and II can be attributed to the different morphological tumor characteristics. Comparison of group II and III reveals the influence of residual tumor after primary surgery.
In conclusion morphometrical analysis correlates with clinical outcome and could be used to increase objectivity of tumor grading and prognosis.

Ova 02

THE SIGNIFICANCE OF PLOIDY AND PROLIFERATIVE ACTIVITY ON SURVIVAL IN OVARIAN CANCER

M.Volm[1], W.Kleine[2], A.Pfleiderer[2], M.Vogt-Schaden (a.G.)[1]

Tumor samples for flow cytometry analysis were obtained from 37 patients with previously untreated ovarian carcinomas of stages III and IV. The nuclear fluorescence of the specifically stained DNA was measured with an ICP-22 pulse cytometer using a mixture of propidium iodide and 4,6-diamidino-2-phenylindole. Seven tumors were classified as tumors with DNA diploidy, 27 as tumors with DNA aneuploidy containing one abnormal DNA stem line and 3 tumors with DNA aneuploidy containing more than one abnormal DNA stem line. The DNA index values range from a value of 1.6 to a value of 5.4. A high stability in DNA content and of the proportion of cell cycle phases was found in primary ovarian carcinomas and their metastases. A relationship between DNA content and distribution of the cell cycle phases was observed. The results of DNA content analysis have prognostic importance with regard to the length of survival time. Patients with aneuploid tumors had significantly shorter survival times than those with diploid or near diploid tumors (p=0.03). Patients whose tumors has a high G0-G1 cell proportion seemed to survive longer than patients with a low G0-G1 cell proportion. If the proliferative pool (S-G2-M-phase cells, ≥17%) of tumors was high, it appeared that the patients died earlier (p=0.09).

Deutsches Krebsforschungszentrum, Institut f. Exp. Pathologie, Im Neuenheimer Feld 280, D-69 Heidelberg 1