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EXPRESSION OF HLA-ANTIGENS ON OVARIAN CARCINOMA CELLS
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The loss of HLA-class I antigen expression on cell surface has implications for the associative recognition of antigenic tumor cells by cytotoxic T-lymphocytes. We investigated the expression of HLA-antigens (class I and II) in ovarian carcinoma cells. For labeling the cell membrane antigen the immunoperoxidase-antiperoxidase slide assay (IPSA) and monoclonal antibodies were used. From 9 solid tumor specimens two cases expressed in all cells HLA-antigens, 7 tumors showed a remarkable variability of positive and negative cells. No HLA-negative cells were seen. In contrast from 10 cases of malignant effusions 4 cases were completely HLA-negative, 4 showed positive and negative cells surfaces, and 2 showed 100% HLA-positive cells. These 2 patients whose tumor cells were labelled completely HLA-positive, CEA-negative and partially Transferrinreceptor-positive showed an unexpected good clinical course. There was no correlation between the expression of HLA-antigens and the histology or the grade of differentiation. In 2 cases with simultaneous testing of primary tumors, abdominal metastases, and the ascites cells an increasing loss of HLA-expression from primary tumor via the abdominal metastasis to the ascites cells was seen. Our findings support the idea of an immunoselection of tumor cell clones. Further investigations must prove the prognostic meaning of HLA-expression in human ovarian cancer cells.

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SIGNIFICANCE OF INTRAOPERATIVE PERITONEALCYTOLOGICAL FINDINGS IN CASES OF MALIGNANT OVARIAN TUMOURS
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Taking into account the histological type, ascites or peritoneal fluid was cytologically investigated in 259 malignant ovarian tumours primarily in stage III. 62,5 % were classified as positive, 2,3 % as unclear and only 2,7 % were insufficient. In the cases of obvious peritonealcarcinosis (n=175) the rate of accuracy was even 75%. There was no difference with regard to the histological type but a surprisingly high rate of accuracy concerning 13 unclassified tumours. Thus a second investigation took into account the degree of differentiation and the clinical stage of 103 patients with serous adenocarcinoma of the ovary.

133 surgical treatments (70 initial laparotomies and 63 second look laparotomies) produced 107 positive histological findings.

In 26 second look laparotomies there was histologically no evidence of disease. In none of the 26 cases peritonealcytology was false positive. On the other hand, 66,3 % of the 107 histological positive cases were found to be peritonealcytologically positive too.

In undifferentiated carcinomas the rate of accuracy ranging 77,4 % was notably higher comparing the 37,5 % of the well differentiated carcinomas. Taking into account the macroscopical findings it was evident that this does not merely result from varying tumourvolumes.

The cases of positive peritonealcytology without obvious peritonealcarcinosis at the initial surgical treatment and macroscopically negativ finding at the second look laparotomy (8 of 22) support the significance of this method with regard to staging and therapy-planing.

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PHASE II TRIAL WITH CARBOPLATINUM (CBDCA, JM8) IN REFRACTORY OR RELAPSED OVARIAN CANCER (OC)

J. Pohl, H.G. Meerpohl and A. Pfeleiderer

Carboplatinum was chosen for clinical studies as one of the most active but less toxic platinum derivative as shown by preclinical trials. Data recently published suggest that advanced OC being resistant to cisplatin may sometimes be sensitive to this platinum analogue. From October 1984 until December 1985 16 pts entered a phase II trial. Patient characteristics are as follows: median age 57 (range 44-66 yrs.), median performance status: WHO grad II, prior chemotherapy: PC 5 pts, PAC 7 pts, therapy without DDP 4 pts; refractory OC 4 pts, relapsed OC 12 pts. Drug dosage used was 400 mg/m² intravenously. Courses were administered in four weekly intervals provided that the pts had recovered from myelotoxic side effects. Pts who had more than 6 weeks between courses will go off study. For evaluation of response the WHO criteria will be used. 5 pts had progressive disease after one cycle and died within 3 months. In the remaining 11 pts, 1 pt with CR, 1 pt with PR and 1 pt with stabilisation of disease (NC) were observed, 8 pts receiving more than 2 cycles showed no response (PD). Toxic side effects: In 39 cycles administered leukopenia (WBC < 2000) occurred in 85% (33/39), thrombopenia (plat < 75000) in 64% (27/39) and anaemia in 82%. Nausea and vomiting were less severe as shown by treatment with cisplatin but were also observed. In 1 pt nephrotoxic side effects were observed (Cr > 1,5). Reduction of dosage was performed in 18 of 39 cycles. In conclusion our preliminary analysis demonstrates, that carboplatinum has some activity in OC pts refractory to standard dose cisplatin but has also dose limiting haematological toxicities. Carboplatinum is relatively free of nephro-, neuro- and ototoxicity.

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PHASE II STUDY OF CARBOPLATINUM/CYCLOPHOSPHAMIDE COMBINATION CHEMOTHERAPY FOR OVARIAN CANCER

H.G. Meerpohl, J. Pohl and A. Pfeleiderer

Carboplatinum (CBDCA, JM-8) is a new but less toxic platinum analogue which seems at least as active against various tumors as the parent compound. Here is reported our initial experience with a phase II study of JM-8 in combination with cyclophosphamide in patients with advanced ovarian cancer. Between October 1984 and September 1985 23 pts suffering from histologically proved epithelial tumors were entered in this trial. When categorized by prognostic factors, 18pts(78%) showed stage III and 5pts(22%) stage IV of disease. Small residual tumor (< 2cm) was observed in 12pts(52%) whereas 11pts(48%) had a large unfavorable postoperative tumorbulk (> 2cm). With regard to histologic grade, 15pts(65%) had poorly differentiated tumors (grade 3). The treatment-scheme consisted of a fixed dose of cyclophosphamide (600mg/m² iv d1) combined with increasing doses of carboplatinum (200-400mg/m² iv d1). There was no pre- or posthydration. The first results which had been observed so far are described below:

JM-8/CYC	CR	PR	NC	PD	NOT EVALUABLE
200/600	-	1	2	3	-
300/600	1	-	3	1	3
350/600	1	1	-	-	5
400/600	-	-	1	-	1

The extent of hematologic toxic effects must be paid attention to because leucopenia (< 1000/mm³) and/or thrombocytopenia (< 25000/mm³) occurred in 16 out of 109 treatment-courses. The myelosuppression however was in general rapidly reversible. The nonhematological toxicity which had been registered was encouragingly low. At the moment our impression is, that carboplatinum in this patient group is tolerated more than cisplatin. The final analysis of the still ongoing trial should clarify the optimal dose of JM-8 in combination with cyclophosphamide and the degree of activity at each dose level.

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