Diagnosis, Treatment and Prognostic Factors in Ovarian Cancer

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CISPLATIN AND TREOSULFANE CHEMOTHERAPY IN THE TREATMENT OF METASTATIC OVARIAN CANCER

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At the Department of Obstetrics and Gynaecology, University Erlangen, 58 patients with metastatic ovarian cancer were treated with a combined chemotherapy of cisplatin and treosulfane.
After primary surgery with maximal tumordebulking patients received 4 cycles of 100 mg/m² cisplatin and 5 g/m² treosulfane in a monthly interval.
After this treatment 46 of the 58 patients underwent a second look operation.
The remissionrate was 81% and 52% of the patients develloped no recurrences or metastases.
The median follow up is 18 months with a variation of 3 - 55 months.
There occured only a small number of serious side effects and mainly due to cisplatin.
Referring to this experience the combination of cisplatin and treosulfane seems to be a promissing chemotherapy in the treatment of metastatic ovarian cancer.

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HIGH DOSE EPIDOXORUBICIN (EPIDX) AND LONIDAMINE (LND) IN PATIENTS (PTS) WITH REFRACTORY OR RECURRENT EPITHELIAL OVARIAN CARCINOMA (EOC).

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High doses EPIDX (150 mg/m²) are effective in pts with EOC pretreated with regimens including cisplatin (CDDP) or carboplatin (CBDCA) obtaining up to 27% response rate (RR). LND is an indazole carboxyle acid derivative that interferes with the multidrug resistance mechanism and enhances cytotoxic activity of EPIDX as shown in vitro and in vivo studies. On these basis we have tested the combination of high dose EPIDX with LND in pts with EOC progressed during or recurred within 6 months after first-line CDDP or CBDCA-based chemotherapy (CT), to asses the antitumor activity and the toxicity of this combination. Up to now 28 pts were treated with LND (150 mg X 3/die orally, day 1 to 5) plus high dose EPIDX (120 mg/m² i.v., day 3) q 3 weeks. All pts are evaluable for toxicity. The most relevant side effect was leukopenia (WHO grade 3-4: 34.6%). Other grade 3 toxicities included: anaemia 15.4%, thrombocytopenia 3.8%, mucositis 7.7%, diarrhoea 3.8%, alopecia 100%. Only 1 pt stopped CT because of cardiotoxicity (decrease in left ventricular ejection rate > 20%). So far 24 pts are evaluable for tumor response: 2 complete responses (8.3%) and 6 partial responses (25%) were observed for a total RR of 33.3%. Six of 8 responding pts were pretreated with antracyclines. In consideration of RR to other second line CT regimens in EOC, the association of LND and high dose EPIDX shows interesting activity.

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MEMBRANE VESICLES RECOVERED FROM THE ASCITIC FLUID OF HUMAN OVARIAN CANCER PATIENTS, CONTAIN COLLAGENASES AND TUMOUR ASSOCIATED ANTIGENS.

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Many kinds of tumour cells are known to shed membrane vesicles in the extracellular medium. These vesicles can be recovered from cell culture medium and biological fluids. Here we report analysis of the morphological appearence, presence of tumour associated antigens and collagenase content of membrane vesicles recovered by ultracentrifugation from ascitic fluids. Vesicles, observed at TME appear very similar to those shed by in vitro cultured breast carcinoma cells (Dolo et al. J. Submicr. Cyt. Path. in press.). They were shown to contain an human ovarian carcinoma associated antigen, the 38 kDa glycoprotein recognized by the monoclonal antibody MOV18, (Miotti et al. Int. J. Cancer 39:297, 1987). Zymographic analyses of vesicles showed the presence of 97 kDa and 72 kDa lytic bands. Lytic bands having similar m.w. had been previously observed in vesicles shed in vitro by breast carcinoma and fibrosarcoma cells.
These results suggest that membrane vesicles can be involved in the metastatic progression of ovarian tumours.

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Aortic infusion (5-FU, MMC, CDDP) and stop-flow (MMC, ADM) for systemically pretreated and progressive FIGO III c and IV ovarian cancer

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18 pts. with progressive FIGO III c (13/18 pts.) and IV (5/18 pts.) ovarian cancer, non responders to prior systemic chemotherapy, underwent regional chemotherapy given via a high aortic catheter in cycle 1 and 2 and aortic stop-flow infusion in cycle 3. Drugs administered were 5-FU (1000 mg), MMC (14 mg) and CDDP (2 x 50 mg), with upper thigh block in the first two courses and 20 mg MMC/50 mg ADM in aortic balloon stop-flow infusion.
14/18 pts. (78 %) had four quadrant and 4/18 pts. had two quadrant peritoneal carcinosis with severe ascites. Pts. FIGO IV showed distant metastasis to the liver and diaphragm (5/5 pts.).
All pts. were resistant to prior systemic chemotherapy and in progression as demonstrated in second look laparotomy (55 %) or CT scan (45 %) before start of regional chemotherapy. Response was estimated acc. to tumor markers, CT scan, reduction of ascites and performance scale.
Overall response was 100 %: 5/18 CR (28 %); 10/18 PR (56 %); 3/18 MR (16 %).
Complete resolution of ascites occurred in 8/18 pts. (45 %), a reduction of > 50 % in 10/18 pts. (55 %).
Tumor markers (CEA, CA 12-5): 5/14 CR (36 %); 5/14 PR (36 %); 4/14 MR (28 %). 4/18 pts. were marker negative.
CT scan: 6/18 CR (33 %); 6/18 PR (33 %); 5/18 MR (28 %); 1/18 SD (6 %).
Median survival was 16.8 mts. 7/18 pts. are still alive for 19.5, 18, 17.5, 17, 16.5, 15 and 12 mts.
Side effects consisting of temporary abdominal discomfort were seldom and usually mild. Severe bone marrow depression was never observed.
Conclusions:
1. In ovarian cancer response is exposure dependent (concentration x time)
2. Regional chemotherapy breaks drug resistance in systemically pretreated ovarian cancer.
3. Patients gain a substantially improved quality of life and survival benefit from aortic infusional chemotherapy.