Ovarian Cancer

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VERY HIGH-DOSE CHEMOTHERAPY (VHDCT) WITH EMATOLOGIC SUPPORT IN PREVIOUSLY UNTREATED ADVANCED OVARIAN CANCER (OVCA): PRELIMINARY RESULTS OF A PHASE I-II STUDY.

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Two consecutive trials were conducted to evaluate a VHDCT programme with autologous bone marrow (ABM) or peripheral stem cell (APSC) support in previously untreated OVCA patients (pts) with macroscopic (0.5-2cm) residual tumor. Fifthy-one pts (median age 44; stage IIIC 78%) underwent: induction chemotherapy (IndCT) (2-4 cycles of a cisplatin and cyclophosphamide combination +/- G-CSF) with ABM and/or APSC harvesting (H) followed by intensification (Int) CT (one course of a platinum, etoposide combination +/- L-PAM,+/-G-CSF&EPO) in the absence of clinical progression. 2nd-look laparotomy was performed in complete responders. 42 (82%) and 39 (76%) pts are evaluable for toxicity and pathological response (pR), respectively while 6 pts are still on treatment, 3 progressed when on treatment, 2 are awaiting 2nd look. One toxic death occurred due to systemic mycosis in a pt undergoing ABM transplantation (T). The number of leukaphereses required for adequate APSCH decreased after G-CSF incorporation. Duration of BM aplasia progressively decreased for pts receiving ABMT, APSCT and APSCT + G-CSF & EPO, respectively. 90% pR (CR 44%, PR 41% of which 36% microscopic) was revealed at 2nd-look. A median follow up of 28 (2-79) months has been reached from diagnosis. Only 2 of the 19 pathologically complete responders (6 with a > 5 year follow-up from 2nd-look) have so far relapsed without further therapy. Treatment proved to be feasible with acceptable toxicity when APSCT + G-CSF & EPO were used. The disease-free interval would seem to be longer than expected in this pt subset. These data, if confirmed after a prolonged observation, warrants further investigation (in a randomized setting) on the possible therapeutic impact of this new approach on chemosensitive tumors.

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RANDOMIZED STUDY OF CYCLOPHOSPHAMIDE, DOXORUBICIN & CISPLATIN (CAP) VS SINGLE AGENT CARBOPLATIN IN OVARIAN CANCER PATIENTS REQUIRING CHEMOTHERAPY: INTERIM RESULTS OF ICON2.

A Crook, on behalf of the International Collaborative Ovarian Neoplasm Studies

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In 1991, a large international trial, ICON2, was launched to compare the CAP regimen with optimal dose carboplatin with the aim of accruing a maximum of 2000 patients worldwide. Parallel trials were coordinated under the same protocol in the UK, Italy and Switzerland. Both arms consisted of 6 cycles of chemotherapy at three weekly intervals. The CAP arm gave cyclophosphamide 500 mg/m^2, doxorubicin 50 mg/m^2 & cisplatin 50 mg/m^2. The carboplatin arm gave a minimum recommended dose of 5(GFR+25) mg, using the AUC method of Calvert et al. (JCO 1987; 7: 1748-1756). An independent Data Monitoring Committee reviewed interim analyses of the data at regular intervals and gave advice on whether the data, together with results from other relevant trials, justified continuing the recruitment of further patients. By the end of September 1995, 1377 patients had been accrued from 140 centres in Italy, the UK, Switzerland, Eire, Poland, Australia, Greece, Singapore and Brazil. The two arms were well balanced regarding baseline characteristics. Compliance with the treatment protocol was good: in both arms 75% of patients received at least 75% of the planned dose intensity and at least 75% of the planned total dose. Patients treated with CAP experienced more severe toxicity overall (WHO grade III or IV): leucopenia 34% vs 10%; thrombocytopenia 7% vs 16%; nausea & vomiting 20% vs 9%; mucositis 21% vs 0%; alopecia 70% vs 3%; cardiac 2% vs 0%; other 2% vs 3%. A total of 526 patients progressed or died, with an 11% reduction in the risk of progression or death in favour of CAP, (95% confidence interval= -6%, 24%, p=0.16). A total of 391 patients have died, with reduction in the risk of death in favour of CAP of 12% (-7%, 28%; p=0.20). Thus currently although there is a slight trend in favour of CAP there is no clear evidence of a difference in effectiveness between the two treatments. The data will be analysed again in October 1996 by which time we expect approximately twice as many events to have occurred.

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Aortic infusion (ADM, MMC, CDDP) and stop-flow (MMC, ADM) for systemically pretreated and progressive FIGO III c and IV ovarian cancer - 45 patients

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45 pts. with progressive FIGO III c (36/45 pts.) and IV (9/45 pts.) ovarian cancer, non responders to prior systemic chemotherapy, underwent regional chemotherapy given via high aortic catheter in cycle 1 and 2 and aortic stop-flow infusion in cycle 3. Drugs administered were ADM (50 mg), MMC (14 - 20 mg) and CDDP (2 x 50 mg) with upper thigh block in the first two courses and 20 mg MMC/50 mg ADM in stop-flow infusion. 36/45 pts. (80%) had four-quadrant and 9/45 pts. (20%) had two-quadrant peritoneal carcinosis with severe ascites. Pts. FIGO IV showed distant metastasis to the liver and diaphragm (9/9 pts.).
All pts. were resistant to prior systemic chemotherapy and in progression as demonstrated in second-look laparotomy (33%) or CT-scan (67%) before start of regional chemotherapy.
Response was estimated according to histology, tumor markers, CT-scan, reduction of ascites and performance scale.
Histological response: 3/21 CR (14%); 8/21 PR (38%); 7/21 MR (34%); 3/21 NR (14%).
Overall clinical response was 91%: 5/45 CR (11%); 21/45 PR (47%); 16/45 MR (35%).
Tumor markers (CA 12-5): 6/34 CR (18%); 16/34 PR (47%); 12/34 MR (35%). 14/48 pts. were marker negative.
CT-scan: 8/41 CR (19%); 10/41 PR (24%); 13/41 MR (32%); 6/41 NR (15%), 4/41 SD (10%).
Complete resolution of ascites occurred in 9/33 pts. (27%), reduction of more than 50% in 14/33 pts. (43%).
Performance improved in 27/45 pts. (60%) and remained unchanged in 9/45 pts. (20%).
Median survival was 12.5 mts., median time to progression 8.6 mts. 12/45 pts. are still alive for 37, 36, 36, 31, 30, 28, 21, 20, 18, 17, 12 and 9 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.

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OVARIAN CANCER IN BULGARIA

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The aim of this study was to analyse the pattern of occurence of ovarian cancer (OC) and mortality from the disease in the period 1983-1992 in Bulgaria. The frequency and trends were studied by age and place of residence of the patients, and histological type of the tumours. Data were provided by the National Cancer Registry and the National Statistical Institute.
Age-adjusted (world standard) incidence of OC has slightly increased during the period. Nevertheless, morbidity increased from 52.4 per 100,000 women in 1983 to 97.6 in 1992 due todecreasing mortality from OC. Age-specific incidence followed similar trends in all age groups.
Serous tumours were the most frequently observed histological type of OC.