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TREATMENT RELATED FACTORS INFLUENCING OUTCOME IN A POPULATION BASED STUDY OF OVARIAN CANCER IN SCOTLAND.

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A population based study of all patients with ovarian cancer registered to the Scottish Cancer Registries in 1987 was undertaken by scrutinizing the case records of 480 patients.

Statistically significant independent prognostic biological variables were age (P<0.001), F.I.G.O. stage (P<0.001), histology (P<0.001), tumour differentiation (P<0.05)and ascites (P<0.01).

Cox's proportional hazard model was used to determine the treatment and management related factors which influenced survival after adjusting for biological factors.

Initial referral to a gynaecologist (P<0.05), initial surgery performed by a gynaecologist (P<0.01), post operative residual disease volume >2cm (P<0.01), management by a multidisciplinary team (P<0.05), platinum chemotherapy (P<0.05) all significantly influenced outcome.

Overall four year survival was disappointingly low at 24% and clearly related to deprivation.

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INTERVENTION DEBULKING SURGERY (IDS) DOES INCREASE SURVIVAL IN ADVANCED EPITHELIAL OVARIAN CANCER (OC): AN EORTC GYNECOLOGICAL CANCER COOPERATIVE GROUP (GCCG) STUDY. Van der Burg MEL, Van Lent M, Kobierska A, Colombo N, Favalli G, Lacave AJ, Nardi M, Renard J, Buyse M and Pecorelli S. Rotterdam Cancer Institute: Daniel den Hoed Kliniek, P.O. box 5201, 3008 AE Rotterdam, The Netherlands.

The question whether the survival benefit of cytoreduction is obtained by the tumour reduction itself or just by selection of good prognostic patients (pts) has never been answered. In 1987 the EORTC/GCCG started a randomized Phase III study with IDS v.s. chemotherapy alone "NO-IDS". Eligible were pts with FIGO stage IIb-IV with tumour rests >1 cm after primary surgery (PS). Pts with a CR, PR and SD after 3 cycles cyclophosphamide/cisplatin (CP) were randomized between "IDS" vs "NO-IDS". All pts received at least 6 cycles CP. 415 Pts have been entered. Not randomized 109 pts: too early 42, PD 29, early death 10, refusal 10, contra-indication for surgery 11, other reasons 7. 306 Pts have been randomized, 151 in the IDS arm and 155 in the NO-IDS arm. Pt characteristics were well balanced between the 2 arms. Response after 3 CP in the randomized pts was cCR 17.5%, PR 54.5% and SD 28%. No mortality nor severe complications due to IDS have been observed. The morbidity observed was similar as after PS. Bladder/bowel injury occurred in 4%, lungembolism and wound infection in 2% each, and thrombosis in 1% of the pts.
268 Pts are available for follow-up (FU), 137 in the IDS and 131 in the NO-IDS arm. The median FU is 30 months (m), maximum FU 56m. Median progression free survival for IDS pts is 16m (range 2.5-54+m), for the NO-IDS pts 12.7m (range 2.5-49,6+m) (p= 0.016). Median survival for IDS pts is 26.3m (range 4-56+m) and for the NO-IDS pts 21m (range 3.5-54.5+m) (p=0.028).
Conclusion: IDS actually improves progression free and overall survival in OC. This study supports the Goldy and Goldman hypothesis. If these data are confirmed by another randomized study, surgery should play a more important role in the treatment of ovarian cancer.

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CHEMOTHERAPY (CAP) FOR THE TREATMENT OF ADVANCED OVARIAN CANCER AND SECOND-EFFORT SURGERY IN THE SECOND-LOOK. A TEN YEARS RESULTS.

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79 patients (p) with advanced ovarian cancer received after the initial surgery five cycles of CAP chemotherapy (CT).
Second-look laparotomy + second effort surgery (SES), p with complete pathological response (CPR) received no futher treatment and p with partial microscopic (PMiR) or macroscopic (PMR) were given 5 more cycles.
Stage III=53 p, stage IV=19, tumor size prior to CT was <2cm in 28 p, 2-5cm in 12p and >5cm in 32. Overall response to CAP was 80%. 16p(23%) obtained CPR, 7(10%) PMiR an 33(47%) PMR. SES was radical in 14/33p with PMR. Ten years actuarial survival (SV) was 27% (median 36 mos). In p with CPR SV rate was 81%, in p with PMiR 43% at 50 m and in p with PMR and radical SES 34% at 72m. Significant differences in survival were found between CPR group and the PMiR (p=0.005). SV was significantly better in patients with PMR where SES was radical (p=0.008) and no different to, p with PMiR.
CONCLUSION: Second effort surgery may be benefitial if all tumor can be excised.

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IS THE " SECOND-LOOK" OLD FASHION ?

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CA 125 Half-Life was studied in 60 patients (pts) with epithelial ovarian cancer. All pts had high CA 125 seric level before initiation of the same cisplatin based combination .
Pts characteristics : FIGO stage : II : 5%, III : 67%; IV : 28%.
Type: serous: 67%, mixed: 7%, undifferenciated: 7%, others :19%.
Grade : 1: 10%, 2: 17%, 3: 60%, unknown : 13%.
Residual disease (RD) at 1st laparotomy : >2 cm: 83%, ≤ 2cm : 17%
RD at 2nd look (RDII): ≤ microscopic: 33%, ≤2 cm: 20%, >2 cm:47%
Results : The median half-life (HL) of CA 125 was 16 days .
Disease free survival (DFS) was significantly different according to whether CA 125 HL was < 15 d or > 15 d, with DFS respectivly of 46 % and 16% at 2 years (p<0.05).
CA 125 HL and CA 125 levels after 3 cycles of chemotherapy (CT) were predictive of 2nd look laparotomy findings :
- If CA 125 is abnormal after 3 cycles, 76% of the pts had RDII >2cm
- If CA 125 HL is > 15 d, 88,2% had RDII > 2 cm
- If both parameters are abnormal, 97,7% had RDII > 2 cm
Conclusion : Combination of CA 125 half-life and CA 125 after 3 cycles, can early select platinum resistant patients for new drugs like taxus derivatives or innovative combination of resistance modulation.

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SECOND-LINE HIGH-DOSE CISPLATIN-BASED INTRAPERITONEAL (IP) CHEMOTHERAPY IN OVARIAN CANCER (OC). van Rijswijk REN, Burger C, Kenemans P, and Vermorken JB. Free University Hospital Amsterdam.

Eighteen OC patients (pts) with small volume disease (<2cm) at second-look or relapse were treated with IP chemotherapy within the context of an institutional phase II study. Their median age was 60 yrs (range 34-72), their median WHO performance status 1 (range 0-2); 14 had received cisplatin before. 13 Pts had residual, 5 recurrent disease (moderately/poorly graded in 4/13 cases). Treatment consisted of 6 cycles of IP cisplatin 200 mg/m^2 & etoposide 350 mg/m^2 with i.v. thiosulphate protection (4 g/m^2 bolus + 12 g/m^2 over 6h) every 4 weeks.
Results: So far, a total of 65 cycles were given (median number of cycles per patient 4, range 1-6). Poor distribution (4 pts), catheter-related problems (3), toxicity (3) and progressive disease (1) precluded full course treatment. 10 Pts had third-look laparotomy. Response data: pathologic (p) CR 4 pts (all with lesions <½ cm), pPR 3, SD 3, PD 2, not evaluable 5, too early 1. Toxicity consisted of nausea and vomiting (severe in 42% of cycles), alopecia, and leukopenia <2x10^9/L (29% of cycles). Only one patient developed WHO grade 2 neurotoxicity. Ototoxicity was minimal. Of 14 pts studied with serial audiography, only 3 showed a mean decrease of > 10 dB over the range of frequencies tested (250-8000 Hz). Median serum creatinine (range) was 91 μmol/L (66-134) before and 110 μmol/L (71-167) after IP treatment. Median survival has not been reached after a median follow-up of 27 months.
Conclusion: although poor distribution and catheter malfunction may preclude full course treatment, high-dose cisplatin-based IP chemotherapy is feasible even after cisplatin containing induction therapy and seems promising.

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A PHASE II STUDY OF TOPOTECAN ADMINISTERED INTRAVENOUSLY AS 5 DAILY INFUSIONS EVERY 21 DAYS TO WOMEN WITH REFRACTORY EPITHELIAL OVARIAN CARCINOMA.

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Topotecan, a new camptothecin analog topoisomerase-I inhibitor, has shown activity in pre clinical and phase I studies. 30 women with ovarian carcinoma refractory to cisplatin and/or carboplatin were treated at starting dose 1.5 mg/m^2/d x 5 days every 21 days. In 28 evaluable patients (pts) the median age was 52 (28 - 76), performance status was 1 (0 - 2), and the median number of prior chemotherapies was 2 (1 - 4). There were 4 (14%) partial responses with a median duration of 8.7 (4.4 - 13.6) months; and 17 (61%) pts with stable disease. The median survival is 14 (2.75 - 16.5) months. The dose limiting toxicity was myelosuppression with a median nadir granulocyte count of 330 cells/μL (12 - 1316) and a median nadir platelet count of 55,000 μL (2,000 - 232,000). The median duration of grade 4 granulocytopenia was 4 days with 58% of pts having therapy delayed, beyond the 21st day, due to persistent neutropenia. One fourth were hospitalized with febrile neutropenia and one third developed a pruritic maculo-papular rash requiring oral steroids. No deaths occurred on study. No significant genitourinary, gastrointestinal, neurologic or cardiovascular toxicity was noted. Topotecan has modest activity in ovarian carcinoma refractory to prior cisplatin and/or carboplatin therapy with dose limiting myelosuppression. The use of cytokines to decrease hematologic toxicity and maintain dose intensity may be warranted.