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IMMUNOCYTOMETRIC DETECTION OF THE α-AND β - ISOFORMS OF DNA TOPOISOMERASE II (TOPO II) IN HUMAN OVARIAN CANCERS

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The relative expression of α- and β-isoforms of DNA topo II is related to the cellular proliferative state. We have performed an immunocytometric investigation of the topo II expression in human tumours. The two isoforms have been detected with specific monoclonal antibodies on cell suspensions. In 20 human ovarian cancers analyzed up to now the isoform-associated immunofluorescence, expressed as α/β ratio, has allowed the definition of at least two different proliferating groups. Values higher and lower than 1 are possibly indicating high and low proliferative activity, respectively. The correlation of this parameter and the clinico-pathological characteristics of this series of ovarian cancers (histology, grading, pathological stage, estrogen-receptor status, response to chemotherapy) is to be investigated.

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A MULTICENTER RANDOMIZED TRIAL COMPARING CYCLOPHOSPHAMIDE +PLATINUM(CP)WITH PLATINUM(P)ALONE IN ADVANCED OVARIAN CANCER(AOC).

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To compare the efficacy of two different regimens of chemotherapy including Platinum,479 patients (pts) with AOC (FIGO stage III-IV) were randomized in a multicenter trial between March 1989 and December 1992. The randomization was centralized and stratified for residual tumor (RT< 2cm =218 pts,RT≥ 2cm=261 pts),performance status and Institution:241 pts were assigned to CP(C=750mg/mq/3w+P=75mg/mq/3w X 6) and 238 to P(50mg/mq/w X 9).Actually 294 pts are evaluable for response (P=151,CP=143) with an overall response (OR)=83.3%.The study is still ongoing;no difference was observed for both schedules of treatment (P 86.1% vs CP 80.4%),particularly a preliminary analysis of the response for RT showed:RT< 2cm=OR P 91.2% vs 83.3% CP,RT≥ 2cm=OR P 81% vs 77.3% CP.Three-year survival rate available in 394 pts is 47.9% (S.E = 4.1)

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CARBOPLATIN, IFOSFAMIDE, ETOPOSIDE, AND GM-CSF IN ADVANCED OVARIAN CARCINOMA, PREVIOUSLY TREATED WITH CISPLATINUM.

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14 patients (pts.) with advanced recurrent ovarian carcinoma previously treated with cisplatinum based chemotherapy, median age 63 (range 36-67) median PS 1 (range 0-2), received Carboplatin 350 mg/m2/d, day 1, Etoposide 125 mg/m2/d, day - 1,2,3; Ifosfamide 1,5 gs/m2/d, day 1,2,3 and GM-CSF 5 ug/kg/d; days 4-10, every four weeks.
All patients are evaluable for toxicity and response, the major adverse effect was granulocitopenia, 9/14 experienced grade 3 granulocitopenia, infection was no observed. No renal, neurologic or hepatic toxicity was encountered.
9/14 pts. had objective response, 4 pts. complete remision and 5 partial remision.
In this heavily pretreated population, with cisplatinum.-Carboplatin, Etoposide. Ifosfamide and GM-CSF exhibited good activity and acceptable toxicity.

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INFLUENCE OF SIZE OF A POSTOPERATIVE RESIDUAL TUMOR ON SURVIVAL OF PATIENTS WITH OVARIAN CARCINOMA, TREATED POSTOPERATIVELY WITH CHEMOTHERAPY

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The size of postoperative residual tumor in patients with ovarian carcinoma is one of the most significant prognostic parameters for further therapy and prognosis. 74 patients with epithelial ovarian carcinoma and evidence of a residual tumor were treated as follows:

1. Cisplatine polichemotherapy (PAC,PC,PA) - 36 patients
2. Alkeran chemotherapy - 34 patients
3. Pelvic irradiation + chemotherapy with Alkeran - 4 patients.

The average follow-up period was 23,2 months, while the median age of out patients was 57 yrs. (26-70). The size of a residual tumor was: up to 2 cm - 4 patients, 2-5 cm -22 patients, more than 5 cm - 48 patients. When tumors up to 2 cm in diameter were in question, there was no use to assess the best mode of therapy, for we had only four such cases.

In the group od 22 patients with a residual tumor being 2-5 cm in diameter, the statistical significance (log rank test) i.e. favourable therapy was Cisplatin polychemotherapy if compared to Alkeran therapy. This group had no cases treated with combined therapy (pelvic irradiation+chemotherapy).

There is no statistically significant difference regarding the aplied chemotherapy in the group of 48 patients with large residual tumors (more than 5 cm. in diameter).

Key words: ovarian carcinoma, residual tumor, chemotherapy

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THE VALUE OF CA 125 AND OTHER CLINICAL VARIABLES FOR THE PROGNOSIS IN OVARIAN CANCER

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After primary operation and chemotherapy the performance of second-look operation (SLOP) is the standard procedure of treatment of patients with ovarian carcinoma. A total of 67 women with ovarian malignancies underwent SLOP. The mean survival rate in patients with negative SLOP was 58 months. In patients with positive SLOP mean survival was 44 and 13 months.when residual tumor at SLOP was <1cm or >1cm, respectively. CA 125 levels measured before SLOP (p=0.0001) and residual tumor after primary surgery (p=0.0001) were significantly correlated with the surgical findings at SLOP. By a multivariate analysis using logistic regression technique formula combining the information CA 125 and residual tumor was constructed. Thus, for patients with primary residual tumor < 2cm and >2cm the probability for a positive SLOP at a tumor marker level of 35 U/ml would be 73 % and 63 %, respectively.

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A PILOT STUDY ON TOLERABILITY OF DOSE INTENSIFICATION OF CARBOPLATIN + CYCLOPHOSPHAMIDE COMBINATION WITH OR WITHOUT G-CSF IN ADVANCED OVARIAN CANCER

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Three dose levels of the combination Carboplatin - Cyclophosphamide were studied in patients with advanced ovarian cancer: Level I (mg/sm) = 300 - 600 (42 patients); Level II = 400 - 600 (9 patients); Level IIIa = 400 - 800 (2 patients); Level IIIb = 400 - 800 + G-CSF at the dose of 300 mg daily s.c. from day 7 to 21 of every cycle (3 patients). Chemotherapy was administered i.v. on day 1 and repeated every 28 days.
Non haematological toxicity was mild not having been observed any grade 3-4 side effect. Median WBC (/cmm) and platelets (x1000/cmm) nadir after the first cycle respectively were as follows: Level I: 3980 - 250; Level II: 3310 - 114; Level IIIa: 1920 - 71; Level IIIb: 2010 - 40.
Recovery on the 28th day was not achieved in 7/42, 1/9, 1/2 and 1/3 patients of dose levels I, II, IIIa and IIIb, respectively.
Thrombocytopenia appears to be the dose-limiting toxicity at dose level III independently of G-CSF administration.