

ability of PBL to TNF production ( $0.25 \pm 0.09$  ng/ml in nontreated group and  $0.15 \pm 0.04$  ng/ml in treated patients). TNF level in tumor culture mediums were found to be similar in the group before ( $0.64 \pm 0.03$  ng/ml) and after ( $0.58 \pm 0.02$  ng/ml) CT.

**Conclusion:** CT modifies TNF level in biological fluids of ovarian cancer patients. This effect could be the result of stimulation of host immune reactions on the diseases and nonspecific cytokine host reaction on CT-induced tumor lysis.

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## PUBLICATION

### Monitoring of CA125 kinetics in prompt evaluation of chemotherapy response of patients with advanced ovarian carcinoma (AOC)

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**Purpose:** The term tumor marker is used as biological marker referring to genetic and biochemical abnormalities in organism, associated with tumor growth, disease status and future tumor behaviour. Perhaps, the most significant role of CA125 is evaluation of initial therapeutic efficacy, i.e. defining of early therapeutic response. CA125 kinetics means spread of normalisation of CA125 during CT.

**Methods:** The prognostic value of serum CA125, both before CT and after each cycle of one of three courses were assessed in 134/237 patients with AOC. All patients received six courses cisplatin polychemotherapy (PC, PA or PAC).

**Results:** Patients with serum CA125 below the normal value of 35U/ml after the first two CT, had significantly longer median survival (101 months) than those when CA125 levels dropped to normal after later courses of CT (21 months) Log rank = 59.9;  $p = 0.0000$ ; Taron-Ware = 58.54;  $p = 0.0000$ ; Breslow = 55.47,  $p = 0.0000$ . Cox univariate analysis confirmed those results: RR = 0.4271 (0.3022–0.6037, CI 95%,  $p = 0.0000$ ). Cox's multivariate analysis verified independent predictive influence of CA125 kinetics on survival: RR = 0.7006 (0.5031–0.9919, CI 95%,  $p = 0.04$ ).

**Conclusion:** Monitoring of CA125 kinetics is much more significant predictor of survival than any initial prognostic factor, such as disease stage, tumor grade, residual disease etc.

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## PUBLICATION

### Role of mammographic screening in ovarian cancer

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**Objective:** Breast cancer is a significant global health problem. It is the most common malignancy in women. Mammographic screening is advised for women older than 40 years for early detection of cancer. The aim of this study is to evaluate the role of screening mammography in ovarian cancer, independent of age.

**Materials and Methods:** Eighty-four patients with ovarian cancer were evaluated with bilateral mammography. Two-hundred healthy controls in the similar age distribution, who were completely asymptomatic, were also imaged with screening mammography. Mammography results were classified according to the "American College of Radiology" criteria in 5 groups.

**Results:** Median age is 51.4 (range, 27–77) and 49.3 (range, 30–75) in patients with ovarian cancer and in healthy controls respectively. Screening mammography revealed 4 malignancy (4.8%) in patients with ovarian cancer; two out of 4 cases were the primary breast carcinoma (2.5%) and the remaining two were the ovarian carcinoma, which metastasized to the breast. Five cases (2.5%) among healthy controls, were also found to have breast cancer.

**Conclusion:** Although the incidence of primary breast carcinoma was found to be similar in two groups (2.5%), mammographic imaging in ovarian cancer patients also helped the diagnosis of metastasis of ovarian cancer to the breast. Therefore, we think that screening mammography should be used in every ovarian cancer patients independent of age.

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## PUBLICATION

### Experience in ovarian cancer primary systemic chemotherapy with cyclophosphamide, epirubicin, carboplatin with concomitant intraperitoneal carboplatin

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**Purpose:** Ovarian cancer is usually treated with debulking surgery and then followed by chemotherapy. The aim of our study was estimation of efficacy of the ovarian cancer primary systemic chemotherapy consisting of carboplatin (CBDCA), cyclophosphamide (CTX), epirubicin (EPI) with concomitant intraperitoneal carboplatin

**Methods:** We enrolled women with ovarian cancer (FIGO II–IV), 70–90% Karnofsky's score. Median age was 55 years (range, 38–77 years). They received a modified regimen consisting of: CTX – 600 mg/m<sup>2</sup> i.v., EPI – 50 mg/m<sup>2</sup>, CBDCA – 400 mg/m<sup>2</sup> plus intraperitoneal CBDCA – 100 mg/m<sup>2</sup>. Median dose of CTX was 877 mg, CBDCA-603 mg, EPI-70 mg, intraperitoneal CBDCA-167 mg. After the surgery all patients received 201 cycles of chemotherapy (median, 6 [range 3–9 cycles] per patient). All investigated women have been assessed with imaging techniques, hematological & biochemical parameters and levels of serum marker – Ca-125. Toxicity was assessed using the WHO score schedule. Moreover, laparoscopic assessment of peritoneal cavity was done when 3 and 6 chemotherapy cycles were completed.

**Results:** In the group of 26 patients we observed: 50% (13) CR%, 42% (11) PR and 8% (2) SD. Overall response rate of 92% (24 females) was observed. Among 4 patients with FIGO II were achieved 3 CR and 1 PR, FIGO III-7 CR, 10 PR, 2 SD; FIGO IV-1 CR, 2 PR. Stable disease was noticed in 2 women after debulking surgery. Median duration of response was 11.6 months (range 1–42+ months). Among the total estimated number of 122 chemotherapeutic cycles we have noticed 40 cases (33%) hematologic toxicities (3rd and 4th WHO degree). Forty cycles have required giving support G-CSF or GM-CSF. One patient had to stop chemotherapy because severe toxicities.

**Conclusion:** These results indicate an important role of systemic chemotherapy combined with intraperitoneal chth in patients with ovarian cancer after debulking surgery.

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## PUBLICATION

### Feasibility of cisplatin (DDP) + topotecan (TPT) combination as second and third line therapy in epithelial ovarian cancer (EOC)

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**Purpose:** We evaluated the feasibility of TPT + DDP in therapy of EOC as second or third line of chemotherapy. This combination is highly effective in vitro but severe hematological toxicity has been reported in vivo.

**Methods:** 14 Patients (pts) have been treated with TPT + DDP (TPT 0.5 mg/sqm/day d.1–5 + DDP 50 mg/sqm d.5 q.3 weeks) as consolidation therapy after a partial response to first line treatment with DDP, Paclitaxel and Epirubicin or Ifosfamide combinations. 10 Pts. were treated with the same schedule as salvage therapy after various lines of treatment containing DDP and Paclitaxel. Treatment was repeated when Absolute Neutrophil Count (ANC) > 1500/mL and Platelets (Plt) > 100000/mL. G-CSF was used after 2 consecutive delays of treatment or in G4 neutropenia lasting more than 4 days. Treatment free interval was 8 weeks in the first group and 60 weeks in the second group of pts.

**Results:** Toxicity per course is summarized in the following table:

		Consolidation (58 courses)	Salvage (41 courses)
WBC	grade 3/4	15/0	1/0
ANC	grade 3/4	12/1	2/1
Plt	grade	3/4	5/1
G-CSF use		4 pts	1 pt

**Conclusions:** The schedule is feasible with a limited use of G-CSF in heavily pretreated patients. Toxicity seems directly related to treatment free interval.