Conclusions: Despite the initial survival advantage observed in irradiated pts, due to late recurrences there was no significant difference in the long-term survival probability of non-irradiated pts. Consolidation whole abdominal irradiation in advanced stages of ovarian cancer may be of value in pts with negative or microscopic disease at SLL.

964 PUBLICATION

Treatment of recurrent ovarian cancer: Intraperitoneal mitoxantrone plus vinorelbine i.v. versus mitoxantrone i.v plus vinorelbine i.v.

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Purpose: To evaluate whether intraperitoneal administration of Mitoxantrone offers any advantage over I.V administration.

Methods: Thirty two (32) women of mean age 65.27 ± 5.13 years with recurrent ovarian cancer were evaluated after treatment (Group A n = 13) with Mitoxantrone (Novantrone, Wyeth-Lederle) intraperitoneally – 36 mg/m" day 1, every 21 days × 6 cycles- plus Vinorelbine i.v. (Navelbine Pierre Fabre) – 37.5 mg/m" day 1 and 8, every 21 days × 6 cycles- or (Group B n = 19) with Mitoxantrone i.v.- 14 mg/m" day 1 every 21 days × 6 cycles – plus Vinorelbine i.v. – 37.5 mg/m" day 1 and 8, every 21 days × 6 cycles.

Results: Response was observed in 6 patients (46.15%) of Group A and in 12 patients (63.15%) of Group B, but this difference was not statistically significant (p = 0.07). There were observed 3/3 pCR in Group A and 6/7 pCR in Group B (p = 0.507). The overall 28 months survival was 76.92% for Group A and 73.68% for Group B (Kaplan-Meier method p = 0.642)

Conclusions: The intraperitoneal administration of Mitoxantrone does not increase the response rate and the overall survival in patients with recurrent ovarian cancer.

965 PUBLICATION

Topotecan (TPT)-based salvage chemotherapy in advanced epithelial ovarian cancer (EOC): A randomized study

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Purpose: In vitro enhanced activity of TPT when combined with Cisplatin (DDP) has been reported. We evaluated the efficacy of TPT vs. TPT + DDP in salvage therapy of EOC after at least 2 lines of chemotherapy contaning DDP and Paclitaxel in a prospective randomized study.

Methods: 18 Pts have been enrolled. 10 Pts received TPT + DDP (TPT 0.5 mg/sqm/day d.1–5 + DDP 50 mg/sqm d.5 q.3 weeks) and 8 had TPT (1.25 mg/sqm/day d.1–5 q.3 weeks). Treatment was repeated when Absolute Neutrophil Count > 1500/mcl and Platelets > 100000/mcl:

Results: In TPT + DDP arm (41 courses) there were 2 grade 3 and 1 grade 4 neutropenia and 2 grade 3 thrombocytopenia; 1 delay of treatment. Out of 10 evaluable pts we had 3 partial responses and 4 stable disease (time to progression 23 weeks, range 9–45).

In TPT arm (27 courses) we observed 8 grade 3 and 4 grade 4 neutropenia, 3 grade 3 and 1 grade 4 thrombocytopenia; 1 delay of treatment. Out of 7 evaluable pts we had 1 partial response and 1 stable disease (time to progression 16 weeks, range 4–28).

Conclusions: DDP + TPT combination seems a very promising schedule worthy of further investigations. Other dose regimens and higher TPT doses may be tested. The study is ongoing.

966 PUBLICATION

Low neurotoxicity of chemotherapy with Carboplatin/Docetaxel for reccurent epithelial ovarian cancer

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The high incidence of peripheral neurotoxicity (PNT) in cisplatin-based chemotherapy for ovarian cancer is often a limiting factor for platinum-reinduction in the case of relapse. Substituting carboplatin for cisplatin in first-line therapy has been shown to decrease the incidence of neurologic and other non-hematologic toxicities without significant difference in tumor response.

In a pilot study, we sought to evaluate the toxicities of a combination of carboplatin and docetaxel in 16 women with relapse of ovarian carcinoma >6 months after completion of first-line platinum-based chemotherapy.

Pts. received carboplatin (AUC5) and docetaxel (75 mg/m^2), i.v., q21. A total of 86 courses was applied. Apart from alopecia, predominant toxicity was hematologic, with WHO grade 2/3 leukopenia in 13/16 and thrombocytopenia in 3/16 pts. Grade 3 PNT was not observed, grade 2 PNT occurred in 1/16 and grade 1 PNT in 12/16 women. 12/16 pts. suffered from mild nausea and vomiting (WHO 1/2), 4/16 from light to moderate fluid retention. Almost all pts. complained of painful, often infectious, changes of finger- and toenails. Ototoxicity and nephrotoxicity were not observed.

9/16 pts. achieved remission with therapy, 2 pts. had NED, 3 pts. stable disease. Five women relapsed within 2 to 9 months after therapy, 2 women progressed under treatment. More complete follow-up data will be available 9/99.

In summary, combination chemotherapy with carboplatin/docetaxel seems an effective treatment for relapse of ovarian carcinoma. Toxicities, especially PNT, tend to be less severe than with cisplatin/paclitaxel. These results warrant larger studies to assess the feasibility of platinum/taxane reinduction for epithelial ovarin cancer with this regime.

967 PUBLICATION

Prognostic significance of heat shock protein (HSP72) immunostaining in epithelial ovarian carcinomas

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Purpose: To evaluate the prognostic value of Heat Shock Protein (HSP) expression in ovarian carcinomas. The correlation between the expression of this protein and the disease parameters: FIGO stage, histological type, tumour differentiation and steroid hormone receptor status (ER, PR) was investigated.

Patients and Methods: One hundred imprint smears from ovarian carcinomas specimens were studied using immunocytochemical techniques. Twenty nine patients were with stage I, 24 with stage II, 40 with stage III kai 7 with stage IV disease according to the FIGO classification.

Results: The sensitivity and specificity of HSP for malignancy was 37% and 90% respectively. HSP was statistically significantly associated with malignant tumours (x^2 = 4.3, p < 0.05) and undifferentiated carcinomas. The relationship of HSP with malignant tumours is confined to the premenopausal group of patients (x^2 = 13.2, p < 0.001).

Conclusion: It can be stated that there is a positive association between HSP positivity in premenopausal patients with malignant ovarian tumours and especially with histologically undifferentiated ovarian carcinomas.

968 PUBLICATION

TNF profiles in ovarian cancer and their response to anticancer therapy

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Purpose: The increased TNF level in biological fluids in ovarian cancer patients has been described earlier. However the contribution by different host and tumor cell populations in general serum and ascite fluid TNF level is not clear, as well as their changes during anticancer chemotherapy.

The TNF levels in ascite fluids, serums, supernatants of 24 h primary ovarian cancer cultures, supernatants of ascite associated peritoneal macrophages (Mp) and peripheral blood lymphocytes (PBL) in 32 cancer patients were determined before any treatment with bioassay using sensitive transformed fibroblasts L-929 cell line. The same parameters were analyzed in 17 ovarian cancer patients after 3–4 cycles (cis-pla-tinum –75 mg/m^2 and cyclophosphomide 750 mg/m^2) preoperative chemotherapy (CT)

Results: TNF serum level was significantly higher in the group with preoperative CT – 0.54 ± 0.08 ng/ml than in serum samples in nontreated patients (0.23 ± 0.03 ng/ml, p ± 0.05). There was the trend to enhance of TNF production by peritoneal Mp after CT (0.32 ± 0.07 ng/ml in treated group and 0.28 ± 0.09 ng/ml in nontreated patients). At the same time common TNF level in ascite fluid was higher in nontreated patients (0.37 ± 0.08 ng/ml) than in group after CT (0.22 ± 0.03 ng/ml). CT decreased the

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

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

969 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 refering 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 therapeutical efficacy, i.e. defining of early therapeutical response. CA125 kinetiks means spreed 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 recived 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 kinetiks on survival: RR = 0.7006 (0.5031–0.9919, CI 95%, p = 0.04).

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

970 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. Sceening 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: Althuogh 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.

971 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 than 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^2 i.v., EPI – 50 mg/m^2, CBDCA – 400 mg/m^2 plus intraperitoneal CBDCA – 100 mg/m^2. 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 casese (33%) haematologic 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.

972 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 ahematological 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	2/0
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.