In conclusion the increase of Carboplatin dose intensity did not improve the antineoplastic effect to any noticeable extent. Further increase of dose intensity cannot be performed without growth factor or stem cell support.

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CARBOPLATIN AND OVARIAN CANCER IN THE ELDERLY

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In western Europe 25% of the population is aged aver 70 years. Half of the new malignancies occur in this group, in general poorly treated. The risk of increased toxicity in relation to the impaired visceral functions, notably renal, requires an individual adjustment of the posology. We have studied the possibility of adjusting the posology of Carboplatin (CBDCA) according to the formula of Calvert: CBDCA DOSE (MG) = 5 (GFR + 25). From Jan. 93 to Dec. 94, 16 elderly women aged between 72 to 85 years with a stage III or IV ovarian carcinoma in good general heath (PS. OMS 0–2) were treated as out-patients by the combination of Carboplatin-Cyclophosphamide every 4 weeks. The number of courses of treatment carried out was between 2 and 6 per patient. An objective response greater than 50% was observed in 14 patients and 2 progressive diseases. 3 patients (73–78 years) have undergone a 2e look and treated by 6 courses of Taxol 175 mg/m^2 every 3 weeks. No grade IV toxicity no hospitalisation due to toxicity.

In conclusion: elderly people should be treated no differently from other age groups, to relieve symptoms, and achieve a cure where possible

—the quality of life must be in mind

—clinical trials should be extended to the elderly.

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TUMOR BULK, HISTOLOGY, AND BASELINE HEMOGLOBIN MAY INFLUENCE RESPONSE (RR) IN PLATINUM PRETREATED OVARIAN CANCER (OVCA)

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Time from last chemotherapy is a well known predictor of RR to 2nd line treatment in relapsed OVCA. Little is known about other tumor or patient (pt) related factors that may be of relevance. For that reason, a multifactor analysis of RR predictors was undertaken in 382 pts enrolled in a European-Canadian trial of 2nd/3rd line paclitaxel. Serous histology, maximum tumor bulk < 5 cm and normal hemoglobin (Hgb) were identified as significant predictors of RR in the final model. To determine if these factors might be of predictive value with other agents, 105 OVCA pts given 2nd line high dose epirubicin in an EORTC GCCG trial were analysed. Results are as shown:

		paclitaxel		high dose epirubicin	
		RR	p value+	RR	p value*
Histology	serous	20.7%	.05	23%	NS
	other	11.8%		17.5%	
tumor	<5 cm	23.9%	.006	23.5%	NS
	>5 cm	12.1%		18.9%	
Hgb	normal	20.7%	.02	23.9%	NS
	low	9.6%		18.6%	
time	<12 mo	15.6%	NS	15.9%	.017
	>12 mo	22.1%		39.1%	

+ final model; *univariate (multifactor analysis not done since only one factor had $P < .05$)

While only time from last treatment reached significance in the EORTC trial, the RR by histology, size and Hgb show the same trends as the paclitaxel trial. Results on other agents will be presented. If higher RR in low bulk disease is consistently noted, a trial of early intervention in relapsed OVCA may be indicated.

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SAFETY AND EFFICACY OF TAXOL® (PACLITAXEL) OVER 3 H IN 306 PLATINUM-REFRACTORY PATIENTS WITH OVARIAN CANCER: RESULTS OF A GERMAN COOPERATIVE STUDY

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We present a phase II study with TAXOL® (Paclitaxel) in 306 patients (pts) with advanced ovarian cancer, who relapsed after at least one platinum based chemotherapy (CT). Objectives are safety and toxicity. Pts received 175 mg/m^2, when pretreated with 1–2 prior CT regimens (Group A: 212 pts, 69.3%) and 135 mg/m^2 with 3 and more CT regimens (Group B: 94 pts, 26.4%) by 3 h-infusion every 3 weeks after standard premedication with steroid, antihistamine and H_2-blocker. The median age was 56 at a performance status of ECOG = 0 in 57.5%, ECOG = 1 in 34.0% and ECOG = 2 in 8.5% of the pts; median time from last CT was 107 days (15–3066). The total number of cycles was 1774, the median number per pt was 6 cycles.

For toxicity data 1202 cycles were evaluated. The main toxicity was neutropenia with higher incidence at 175 mg/m^2 (WHO 1 + 2: group A: 63.3%, group B: 71.2%, WHO 3 + 4: group A:36.7%, group B: 28.8%;), which is not statistically significant.

Thrombocytopenia: WHO 1 + 2: A: 1.8%, B: 1.3% WHO 3 + 4: A: 15.7%, B: 13.8%.

Anemia: WHO 1 + 2: A: 17.8%, B: 19.9%. WHO 3 + 4: A: 1.8%, B: 1.2%.

Non-hematological toxicities were minimal:

Arthralgia/myalgia: WHO 1 + 2: A: 19.1%, B: 14.0%. WHO 3 + 4: A: 2.4%, B: 2.6%

Peripheral neuropathy: WHO 1 + 2 A: 36.0%, B: 19.2%. WHO 3 + 4: A: 0.4%, B: 0.9%.

Alopecia.: WHO 1 + 2: A: 26.7%, B: 24.2%. WHO 3 + 4: A: 69.5%, B: 71.7%.

Hypersensitivitity reactions: WHO 1 + 2: A: 17.2%, B: 8.3%. WHO 3 + 4: A: 0.3%. B: 0.0%.

295 pts could be evaluated for response: complete response (CR): 28 pts (9.5%), partial response (PR): 57 pts (19.3%); stable disease (SD): 119 pts (40.3%) and 85 pts (28.8%) with progression.

This study confirmed the efficacy and tolerability of TAXOL®, administered as 3-h-infusion after premedication, in the treatment of platinum-refractory ovarian cancer. Main toxicity was neutropenia without severe clinical manifestations. The encouraging response rate for these heavily pretreated patients will lead to further studies in first-line ovarian cancer.

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CLINICAL RESULTS OF A NEW APPROACH OF THERAPY OF OVARIAN CANCER: RETARGETING OF T CELL CYTOTOXICITY BY BISPECIFIC ANTIBODIES

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We propose specific retargeting of *in vitro* activated PBMC by an anti FBP/antiCD3 bsAb (OCTR) as an alternative to second-line conventional treatment of ovarian carcinoma. 28 patients with limited i.p. disease after surgical debulking were studied. They received 2 i.p. 5-day cycles of activated PBMC retargeted with OCTR plus low-dose r-IL2. Despite unfavorable tumor characteristics i.p. CR or PR in 9 of 27 patients (33%) were demonstrated by strict surgicopathologic evaluation methods. In most of the responding patients, the disease relapsed outside the peritoneal cavity and in 2 cases CR i.p. were accompanied by progression in retroperitoneal lymph nodes, suggesting that this form of treatment is active in a local fashion.

To possibly cure extra peritoneal disease, we started clinical safety studies to establish the appropriate dosages of i.v. infusion of OCTR coated T-lymphocytes. In 3 patients which received simultaneous i.v. and i.p. infusions, signs or symptoms were not significantly different from those observed after i.p. treatment. Immunological monitoring and clinical evaluation are ongoing. Partially supported by CNR-ACRO end AIRC.