the first day with 3 weekly intervals. Patients without a definite clinical or radiological evidence of disease progression underwent surgical laparotomy for response assessment.

Results: Pathologic complete response was attained in 19 pts. (73.1%). One patient (3.8%) had progressive disease. After a median follow-up period of 29 months (10-64), 13 pts. (50%) are alive with no evidence of disease, 4 pts. (15.4%) are living with their underlying disease and 9 pts. (34.6%) have died due to tumor progression. Median response duration in those with primary and persistent disease are 17 months (0-48) and 12 months (0-40), respectively. Out of 205 cycles, WHO grade III and IV toxicities were documented as follows: anemia 3 pts (11.5%), neutropenia 2 pts. (7.7%), thrombocytopenia 2 pts. (7.7%), emesis 6 pts. (23.1%), renal toxicity 3 pts. (11.5), diaarhoae 1 pt. (3.8) and alopecia 17 pts (65.4%). A neutropenic febrile episode was observed in 1 patient. Intraperitoneal treatment caused grade III abdominal pain in 3 patients.Three pts. (11.5%) had catheter-related complications; which necessitated an alteration to intravenous (IV) cisplatin treatment in 2 pts. In 3 pts. intraperitoneal cisplatin had to be replaced by IV carboplatinum due to severe nephrotoxicity. There were 4 cycles of treatment delays due to hematologic toxicity in 2 pts., nephrotoxicity and severe emesis in 1pt. and an autitis episode in 1 pt.

Conclusion: Intraperitoneal cisplatinum combined with IV paclitaxel at 135 mg/m2 as a 3 hour infusion is an effective and safe combination for the treatment of advanced ovarian cancer.

1197 POSTER

Independent prognostic factors who predicted progressive disease in advanced ovarian cancer

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This study was undertaken to assess the prognostic value of thirteen variables in 222 patients with advanced ovarian cancer related to the interval to progression.

Besides the pretreatment CA125 values, marker kinetiks and CA125 half-life (T1/2), ten other common clinicopathological variables were investigated: age, type of surgery, disease stage, Karnofsky index, residual disease, histological type, histological grade, type of cisplatin chemotherapy (PAC, PC, PA), number of chemotherapy cycles (CT) and treatment response.

Serial determination of tumor marker CA125 were performed in all patients. T1/2 was calculated in 122/222 patients, according to the van der Burg's formula. CA125 kinetics could be estimated only for patients whose prechemotherapy levels were above 35 U/ml, i.e. 134/222 patients.

A univariate analysis (log-rank, Tarone-Ware, Breslow and univariate Cox analysis) estimates the effect of each prognostic factor individually, not taking into consideration coexisting prognostic factors. Statistical significance was observed for the following out of 13 investigated variables: age, type of surgery, FIGO stage, histological grade, residual disease, Karnofsky index, number of chemotherapy, CA125 kinetics and C A125 half-life (T1/2). A multiple regression analysis based on Cox's proportional hasard model was used to test the relative importance of variables as predictors of free interval to progression. The indipendent predictors in order of significance are: Karnofsky index ($p<0.0001$), T1/2 ($p=0.0011$), CA125 kinetics ($p=0.0014$), histological grade ($p=0.0087$) and residual disease ($p=0.0191$).

As consequence, the possibility to predict treatment response by the CA125 half-life during CT and the time need for normalization of CA125 levels can divide patients into good and poor prognostic group early during CT.

1198 POSTER

Are p27,p21 and p53 prognostic factors in ovarian carcinoma patients?

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p21, p27 and p53 have been shown to be of prognostic significance in different human tumors.

Material and methods: Using immunohistochemistry, we examined p27, p21 and p53 in a series of 76 consecutive SEN (Serous Epithelial Neoplasia) pts. Thirteen borderline tumors were excluded from this analysis, leaving 53 primary ovarian (31 serous papillary, 22 other histotypes) and 10 serous surface papillary carcinomas, with a median follow-up of 38 months (range: 2-84).The carcinomas were graded according to WHO (3 G1, 33 G2, 19 G3 and 8 G4) and staged according to the FIGO criteria (24 S I-II and 39 S III-IV).Immunostaining monoclonal antibodies were K2502 (p27), EA10 (p21) and DO7 (p53).Cases were considered positive if the percentage of stained tumor cells was above the median value of 20% for p27 and p53, and 2.5% for p21.

Results: Among the 63 evaluable tumors, 55.5% showed a clear p53 overexpression and 49.2% showed low p27 and p21 expression.

No relation was seen neither between p53 and p21 nor between p27 and p21.

No significant relation was also observed between these markers and tumor histotype, grade or stage, although a trend was seen for higher grade tumors to overexpress p53.DFS and OS appeared to be correlated with grade ($p=0.02$ and $p=0.01$), stage ($p<0.0001$ and $p=0.004$) and p53 expression ($p=0.03$ and $p=0.02$), but not with the combined p53/p21 phenotype.At 4 years, DFS and OS were statistically worse (30% and 56%) in p53 positive tumors than in p53 negative (61% and 75%).

Conclusions: these data appear to confirm the worse prognosis of p53 overexpressing ovarian cancers, while p21 and p27 don't seem to correlate with clinical outcome.

1199 POSTER

A phase II trial of a paclitaxel and oxaliplatin combination in advanced ovarian cancer patients pretreated with cisplatin or carboplatin ± taxanes: Preliminary results

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Purpose: The aim of this ongoing study is to evaluate the efficacy and safety of a paclitaxel and oxaliplatin combination in patients with advanced ovarian cancer (AOC) and clinically measurable disease, pretreated with one platinum based regimen ± taxanes, with a platinum-free interval of at least 6 months.

Patients and Methods: As of March 2001, the first 24 patients (pts) entered in 9 French centers had been externally reviewed. Median age was 61 years (40–76), and performance status was 0 = 12 pts, 1 = 9 pts, 2 = 3 pts. Platinum free interval (PFI) was >12 months in 16 pts, and 6–12 months in 8 pts. Paclitaxel 175 mg/m^2 was administered over 3 h followed by oxaliplatin 130 mg/m^2 over 2 h every 21 days for a maximum of 6 to 9 treatment cycles.

Results: Twenty-two pts (115 cycles) were eligible and evaluable for efficacy and toxicity, 14 of whom were taxane-pretreated. An ORR of 91% was achieved with CR observed in 5 pts, PR in 15, and SD in 2. Median follow up was 7 months (4–16); 6 pts progressed (at 7, 7, 8, 10, 11, and 12 months), and no deaths occurred. The median number of cycles received was five (2$^+$–9). Grade 3 and grade 4 neutropenia occurred in 33% and 13% of cycles, respectively, with a single episode of febrile neutropenia. Grade 3 thrombocytopenia was observed in 1% of cycles, grade 3/4 nausea and vomiting in 3%, grade 3 asthenia in 4%, and grade 3 allergic reaction in 2%. Reversible neurotoxicity ≥ grade 2 (NCI-CTC) was observed in 54% of pts after a median of 4 cycles (3–6) and led to treatment discontinuation after six cycles for one patient.

	Prior taxanes	N = 14	No prior taxanes N = 8		Total (N = 22)
PFI (months)	6–12	>12	6–12	>12	-
CR + PR (pts)	6	7	1	6	20 (91%)
SD (pts)	1	–	–	1	2 (9%)

Conclusion: These encouraging results indicate that the paclitaxel and oxaliplatin combination is safe and very active in platinum-pretreated AOC patients with a platinum-free interval of at least 6 months.

1200 POSTER

Relapsed ovarian cancer after failure of first-line chemotherapy with platin and paclitaxel -a phase II study

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Background: Topotecan (T), a topoisomerase I- inhibitor, is approved for