All pts had received prior treatment with platinum containing combination chemotherapy.

**Results:** The median P dose/week received for P70 (57 pts) was 42 (24–52.5) mg/m²/wk, for P50 (35 pts) it was 32 (20.6–37.5) mg/m²/wk. The WBC nadirs were median 1 85 (0.64–8.9) × $10^9$/l and 2 1 (0.75–4.9) × $10^9$/l and the Plts nadirs were median 67 (8–193) × $10^9$/l and 127 (11–320) × $10^9$/l, respectively. 5 P70 pts had nephrotoxicity grade 2. Neurotoxicity grade 2 was observed in 4 P70 pts and 3 P50 pts. The response rate according to the PFI is shown in the table.

| Response | PFI < 3 m N = 22 | PFI 3–6 m N = 14 | PFI 6–12 m N = 21 | PFI > 12 m N = 35 |
|---|---|---|---|---|
| CR | 18% | 22% | 33% | 57% |
| PR | 18% | 57% | 62% | 34% |
| Overall RR | 36% | 79% | 95% | 91% |

The response duration for the patients with a PFI of <1 year was median 10 m, range (4–29⁺)m and for pts with a PFI ot of >1 year median 14 m, range (3.5–29⁺)m.

**Conclusion:** Salvage therapy with weekly cisplatin and oral vepesid is highly active Combination chemotherapy with weekly cisplatin should be tested in first-line.

530 ORAL

## Efficacy of a combination of irinotecan (CPT-11) with mitomycin-C (MMC) for clear cell carcinoma of the ovary (OCCA) which is intrinsically platinum-resistant

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**Purpose:** To assess the efficacy of a combination of CPT-11 with MMC for OCCA which is intrinsically platinum-refractory.

**Methods:** Eligible patients (pts) had histologically-confirmed pure OCCA progressed during platinum-based chemotherapy (CTX) or relapsed within 6 months after the end of this CTX, measurable lesions, WHO PS ≤ 3, age ≤75, adequate hematopoietic, liver and renal functions, and written informed consent.

Protocol: CPT-11 (140 mg/m², IV infused over 4 hours on day 1, 15, and 29) and MMC (7 mg/m², IP injection through a reservoir on day 1, 15, and 29). The course was repeated every 3 weeks.

**Results:** To date 24 pts with OCCA were entered, of whom 7 had failed to respond to prior CPT-11 alone subsequent to platinum-based CTX. The median age was 53 (40–69). Among total 73 courses, grade 3 diarrhea was observed in 8 courses. Other toxic signs were acceptable. The responses by tumor size were 2 CR, 2 PR, and 1 NC for ≤2 cm in diameter, and 2 CR, 5 PR, 9 NC, and 3 PD for >2 cm. Eleven responders have showed a significantly longer survival compared with 13 non-responders (median survival after the start of CTX: 21 months vs 8 months, p < 0.001 for Log-rank test).

**Conclusion:** CPT-11 plus MMC was the first regimen to demonstrate a significant activity with survival benefit for intrinsically platinum-resistant OCCA. Further studies with this regimen are warranted in previously untreated pts with OCCA.

531 ORAL

## Cisplatin/paclitaxel vs carboplatin/paclitaxel: Optimizing of treatment in advanced ovarian cancer

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**Purpose:** Recently, it has become evident that in advanced ovarian cancer primary chemotherapy with Paclitaxel/Cisplatin is more effective than the combination Cyclophosphamide/Cisplatin. An issue that has to be addressed is to decrease the severity of side effects by substituting the nonneurotoxic analogue carboplatin for cisplatin.

**Methods:** Patients FIGO stage IIb–IV were randomised to two treatment arms receiving either Paclitaxel 185 mg/m² plus Carboplatin AUC = 6 mg/ml/min (Arm A) or Paclitaxel 185 mg/m² plus Cisplatin 75 mg/m² (Arm B). 6 cycles were administered every 3 weeks. Patients followed stratification of <1 cm vs. >1 cm residual tumor.

**Results:** After 12 months 382 patients were enrolled in the ongoing study protocol Hematological toxicity occurred more frequently in Arm A, febrile neutropenie > grade 2 was not observed. G-CSF, antibiotics or red blood cells were given in less than 4% of courses in both arms. Treatment delay ≥7 d was observed in 13% and 7% in Arm A and Arm B, dose reduction was necessary in less than 5% of courses in both arms. Grade II neuropathy occurred in 17% and 33% of pts. in Arm A and Arm B, respectively.

**Conclusion:** Accrual is still going on. Except for alopecia, non-hematological toxicity occurred more frequently in Arm B.

532 ORAL

## Long term survivors from a European-Canadian trial of paclitaxel in platinum-pretreated ovarian cancer (OVCA)

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In a randomized European-Canadian study, 2nd or 3rd line paclitaxel (P) was given to 391 pts with recurrent OVCA. Results of the trial comparing two doses and schedules of P have been reported (JCO 12: 2654, 1994). Long term data indicate 65 pts lived >2 yrs after receiving P. In order to determine if pt characteristics at study entry were related to likelihood of long survival (LTS), both groups were compared with respect to 23 baseline variables Univariate results are shown:

| | >2 yr survivors (n = 65) | <2 yr survivors (n = 326) | p value |
|---|---|---|---|
| Mean age (yrs) | 53.1 | 56.7 | 0.018 |
| Performance status 0 | 60% | 37% | 0.001 |
| Histology serious | 66% | 55% | 0.095 |
| Mean size largest lesion (cm) | 6.6 | 7.8 | 0.029 |
| ≤2 sites of disease | 82% | 53% | 0.001 |
| CR to first-line chemo | 46% | 30% | 0.013 |
| Days since diagnosis (mean) | 993 | 647 | 0.0003 |
| Days since last chemo (mean) | 406 | 215 | 0.0003 |

Following stepwise logistic regression, 4 factors remained significant at p < 0.05: age, number of disease sites, time since last chemo and performance status. Since all pts received P, no conclusion can be drawn regarding its impact on LTS, but these data suggest pt and disease characteristics at the time of initiation of 2nd or 3rd line OVCA treatment have an important effect.

533 POSTER

## Independent radiological review of a phase III study of topotecan versus paclitaxel as second-line therapy in advanced epithelial ovarian cancer

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**Purpose:** To independently review claimed responses in a randomised, multicentre trial of topotecan (T) vs. paclitaxel (P) for advanced epithelial ovarian cancer (AEOC).

**Methods:** 226 patients (pts) with bidimensionally measurable AEOC, who had failed prior platinum-based therapy, were randomized to receive either T (1.5 mg/m²/d × 5 as a 30 min. inf. q 21 d) or P (175 mg/m²/d as a 3 h inf. q21 d). Pts who progressed or whose best response was stable disease after 6 courses were eligible to receive the alternate regimen. Radiographs or scans for claimed responses were reviewed by an independent radiologist.

**Results:**

| Randomised Treatment | Topotecan | | Paclitaxel | |
|---|---|---|---|---|
| | No. randomised | No. Switched to P | No. randomised | No. Switched to T |
| No. of pts | 112 | 60 | 114 | 48 |
| Claimed responses | 38 (37.9%) | 6 (10%) | 28 (24.6%) | 2 (4.2%) |
| Confirmed responses | 23 (37.9%) | 6 (10%) | 16 (14.0%) | 2 (4.2%) |
| No. rejected | 15 | 0 | 12 | 0 |
| % Rejected of claimed | 39.5% | 0% | 42.9% | 0% |

Independent radiological review rejected 35% of responses; reasons for rejection included misinterpretation of normal structures & measurement errors.

**Conclusions:** T is an active agent in AEOC & although independent radiological review reduces the response rate it verifies the accuracy and