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## Paclitaxel, Ifosfamide and Cisplatin (TIP) chemotherapy for recurrent or advanced squamous cell cervical cancer (SCCC)

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**Background:** Salvage chemotherapy for recurrent or persistent SCCC yields unsatisfactory results. Cisplatin is the most effective drug but Paclitaxel and Ifosfamide have recently been tested with promising results.

**Methods:** 45 Patients (pts) with recurrent or persistent SCCC underwent treatment with TIP (Paclitaxel 175 mg/sqm d.1, Cisplatin 50 mg/sqm d.2, Ifosfamide 5 g/sqm d.2, MESNA 5 g/sqm d.2 and 3 g/sqm d.3) from 4/1996 to 2/1999. 25 Had received prior irradiation. A minimum of 3 courses were planned.

**Results:** 3 Pts are under treatment and 42 have completed the treatment. Two pts required early discontinuation of treatment (1 severe myelotoxicity, 1 acute hepatitis), leaving 40 pts evualuable for response. In all 180 courses were administered. We observed 14 clinical complete responses (CR 35%), 15 partial responses (PR 37%), 5 stable disease (SD 12%) and 6 progressions (PD 15%). 7 Pts with CR underwent surgery and 5 had pathologically confirmed CR. The median survival is 13+ months (m) in pts with CR, 11+ m for PR, 6 m for SD and 4 m for PD. The response rate was 62% in irradiated areas and 79% in non-irradiated areas. Toxicity was relevant, with G3–4 myelotoxicity in 90% of pts and G3 renal toxicity in 5% of pts. One case of life threatening toxicity was recorded.

**Conclusions:** These results need to be confirmed in larger study populations but are extremely promising. This regimen could provide better control of persistent-recurrent SCCC than currently available combinations. The toxicity is acceptable.

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## Outcome in patients who become pregnant within 12 months after completing single and multiple agent chemotherapy for gestational trophoblastic disease (gtd)

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**Purpose:** Patients who have completed chemotherapy for GTD are advised to avoid pregnancy for 12 months because: (1) the rising hCG of pregnancy will mask a relapse which is most likely to occur in the first year; (2) chemotherapy may predispose to increased teratogenicity; (3) pregnancy hormones may actually drive recurrence of GTD. Here, we examined the effect of early pregnancy on the relapse rate and fetal outcome following treatment for GTD.

**Method:** The Charing Cross GTD database was screened to identify all treated patients who had either completed single drug or combination drug therapy.

**Results:** 1456 patients were treated for GTD between 1973 and 1997 at our center. Of these 677 received single drug (SD) and 779 combination drug (CD) therapy. 79 patients subsequently relapsed, of whom in the first 12 months 3.4% (23/677) had SD and 4.6% (36/779) CD therapy. In agreement with our previous data, 75% (59/79) of these relapses occurred within 12 months of completing initial treatment. Despite advice to avoid pregnancy in the first year following therapy, 147 patients in the SD and 83 from the CD groups became pregnant within 12 months. Only 2.2% (5/230) relapsed, of whom 3 (2%) originally received SD and 2 (2.4%) CD treatment. Interestingly, 72% (166/230) had a healthy infant with no fetal abnormalities recorded. Other outcomes included elected terminations in 25% (57/230), still births in 2% (4/230) and new molar pregnancies in 1.5% (3/230).

**Conclusion:** While we continue to advise patients to avoid pregnancy in the first year following treatment for GTD, those that do conceive can be reassured of a likely favorable outcome.

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## Carboplatin alone (C) vs carboplatin + high-dose epirubicin (HDCE) in late recurrent ovarian cancer patients (PTS)

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**Purpose:** To evaluate the efficacy of Carboplatin (C) alone vs C plus High-Dose Epirubicin (HDCE) in the treatment of late recurrent ovarian cancers we conducted a randomized clinical trial.

**Methods:** From 1991 to 1998 a total of 187 pts, median age 55 years (range 27–75), with late recurrent (>6 months after first line chemotherapy with complete or partial response) ovarian cancers were randomly allocated to C alone (93 pts, C = 300 mg/sqm q 4 wks × courses) or C + HDCE (94 pts, C = 300 mg/sqm q 4 wks + E = 120 mg/sqm q 4 wks × 5 courses) + GM-CSF (5 gr/kg o.d. × 11 days). All randomized pts performed a previous cisplatin or carboplatin based chemotherapy regimens as first line without anthracyclines. According to first chemotherapy 60 pts achieved a complete remission (CR), and 44 an optimal partial response (residual tumor < 1 cm); the median progression free interval was 23 mos (range 6–144). Pts categories were balanced in the two arms.

**Results:** The 3-years cumulative survival was 49% (SE. 1.0) in women allocated to C alone and 56% (SE. 1.0) in women allocated to C + HDCE. This difference however was not statistically significant. Toxicity was evaluated according to WHO grading (%). Haematological toxicity was more frequent in C + HDCE than in C alone group: leukopenia G0, G1, G2 and G3, G4 respectively 46 and 53 for C + HDCE group and 87 and 13 for C alone; thrombocytopenia G0, G1, G2 and G3, G4 36 vs 64 and 80 vs 20, anemia 66 vs 44 and 90 vs 10. These differences were statistically significant. Nausea and emesis were mild in both groups while alopecia G3 was present in the 88% of C + HDCE pts.

**Conclusions:** This randomized trial on efficacy of two different second line treatments for sensitive relapsing ovarian cancers shows that women treated with C alone or C + HDCE achieved similar 36 month survival rates. Toxicity was significantly higher in women treated with C + HDCE.

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## Treatment of patients with advanced ovarian cancer (FIGO IIb–IV) with cisplatin/paclitaxel or carboplatin/paclitaxel – An interim analysis of the ago study protocol ovar-3

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**Purpose:** The AGO-Study Group Ovarian Cancer started a protocol to evaluate the best combination of paclitaxel with either one of the platinum compounds.

**Methods:** Between 10/1995–11/1997 a total of 798 patients were randomized to two treatment arms receiving either paclitaxel 185 mg/m$^2$ + cisplatinum 75 mg/m$^2$ (arm A) or paclitaxel 185 mg/m$^2$ + carboplatin AUC 6 (arm B) according to the Calvert formula. Patients followed stratification of favourable (<1 cm) and unfavourable (>1 cm) residual tumor. Progression-free survival (PFS) is the primary study goal, whereas the median overall survival (OS) and quality of life measured by the EORTC QLQ-30 questionnaire represent secondary parameters.

**Results:** 783 patients who received 4361 cycles were eligible with a median follow-up time of 2 yrs.. Both regimen showed similar effectiveness concerning PFS and OS ($p > 0.05$). Full dose intensity could be administered in 94% (arm A) and 96% (arm B), respectively. In the latter arm grade III/IV myelosuppression was observed more frequently (14% vs. 8%), but without clinical symptoms. Emesis (19% vs. 7%) and neuropathy (19% vs. 8%) were significantly detected more often in arm A. In those patients quality of life was significantly worse ($p < 0.001$).

**Conclusions:** As carboplatin/paclitaxel shows similar effectiveness but less toxicity related to the quality of life this regimen is considered as the current standard chemotherapy in patients with advanced ovarian cancer.