the treatment of recurrent ovarian cancer, and Gemcitabine (dFdC) has also shown demonstrable activity against ovarian cancer. Both drugs affect DNA synthesis, and in addition, Topotecan, inhibits DNA repair. We performed a monoinstitution dose-finding study with T administered on d1-d5 and dFdC on d1+8/q22d as 30 min infusion without growth factors (ASCO 1999, *1482).

**Methods:** For this multicenter phase II study patients with relapsed epithelial ovarian cancer and prior treatment with platinum- and paclitaxel-containing chemotherapy, ECOG status 0-2 were eligible. All patients gave their written informed consent. T was given at a initial dose of 0.5mg/m2/d and dFdC of 800mg/m2 on day 1 and 600mg/m2 on day 8.

**Results:** From 3/1999 to 1/2000 21 patients (median age 58 years, range 36-70) with 1-3 pre-treatments were recruited. Ninety-four courses (median: 6; range:1-8) have been applied. The topotecan dosage has been escalated to 0.75 mg/m2 after the first course in eight patients, in two patients to 1.0mg/m2 topotecan. Dose reduction was not necessary in any case. Only 1 patient developed leucopenia CTC-grade 4 after the first cycle, while 3 patients suffered from grade III/IV anaemia. There were no episodes of neutropenic fever, sepsis or chemotherapy-related fatalities. Four patients experienced thrombocytopenia grade IV but without clinical sequelae. The incidence of non-haematological toxicities was very low. Grade 2 alopecia occurred in ten cases. Ten patients were evaluated for clinical tumour response by standard radiographic methods: 3 CR, 4 PR, 1 SD, 2 PD. No evidence of disease (NED) was observed in four and 7 patients were not evaluable for response. With a mean follow up of 15 months the median disease free survival of patients was 8.8 months (95%CI 8-9.5) and the mean 10.4 months (95%CI 7.4-13.3). The median of overall survival has not yet been reached with a mean overall survival of 18.6 months (95%CI 15.3-21.9). 14 of patients are still alive.

**Conclusion:** Topotecan in combination with Gemcitabine had a favourable toxicity profile and showed encouraging response and survival. A phase III study to compare a mono- with a combination chemotherapy has been started. Supported by SmithKline Beecham Germany

1201 POSTER

## Topotecan (T) and cyclophosphamide (CY) in second line treatment of advanced ovarian cancer (AOC): a gineco phase II trial

F. Mayer, P.Y. Peaud, J.D. Tigaud, M.C. Kaminsky, S. Culine, S. Walter, H. Barletta, P. Bastit, J.M. Vannetzel, E. Pujade-Lauraine. *Gineco, Group, Paris, France*

**Purpose:** Based on in vivo studies showing synergy between T and Cy and on a previous phase I study (Murren et al, J Clin Oncol 148-157, 1997), the GINECO group initiated a phase II trial to investigate the efficacy and tolerance of combined T and Cy in patients (pts) with recurrent AOC treated with only one previous platinum and taxane based regimen.

**Methods:** From 08/98 to10/00, a total of 86 pts received a q3 weeks schedule of T (0,75 mg/m2/d) for 5 consecutive days and Cy (600 mg/m2/d) on day 1.

**Results:** Pts characteristics were the following: age (median 60 yrs, range 33-79), serous histology (60%), PS 0-1 (95%), chemosensitive disease (DFI >6 months)(58%), measurable tumor (50%), CA 125 level >40 UI/ml (88%). Pts received a median of 4.5 courses (1-9). Hematologic toxicity was NCI grade 3-4 neutropenia (59% of cycles), thrombocytopenia (9%) and anemia (18%). Febrile neutropenia occurred in 8%. G-CSF, red blood cell and platelet transfusions respectively were required in 17%, 15% and 1%. Dose reduction and course delay were observed in 9% and 20%, mainly due to hematological toxicity. Non-hematological toxicity was moderate except alopecia (49%) and grade 3 fatigue (19%). To-date 80 pts are evaluable yielding an overall response rate of 24% (19/80) including 3 pts (4%) achieving clinical complete remission. Response rate is 3% in pts with <6 months relapse (1/35) and 40% in chemosensitive disease (18/45). Median progression-free survival and overall survival is respectively 5 and 10 months.

**Conclusion:** the combination of T and Cy is feasible and tolerable in outpatient treatment of recurrent AOC. T+Cy combination achieves an encouraging 40% response rate in pts with relapse >6 months after platinum and taxane treatment.

1202 POSTER

## Topotecan and paclitaxel in second line treatment of advanced ovarian cancer (AOC): a gineco phase II trial

M. Fabbro, B. Leduc, L. Mignot, P. Ayela, D. Assouline, M.C. Gouttebel, D. Lebrun-Jezekova, S. Walter, D. Paraiso, E. Pujade-Lauraine. *Gineco, Group, Paris, France*

**Purpose:** Topotecan (T) and Paclitaxel (P) have been demonstrated to be effective in second line treatment of ovarian cancer and are among the two best candidates for a non-platinum doublet in the treatment of AOC.

**Methods:** A total of 34 patients (pts) with recurrent AOC after a previous platinum-based regimen without taxane received a q3w schedule of T (0,75 mg/m*/d, d1-5) and P (135 mg/m*, 3 hours, d1).

**Results:** Pts characteristics were age (median 59 yrs, range 40-74), serous histology (65%), PS 0 (59%), platinum-sensitivity (DFI >6 months) (70%), measurable tumor (71%), CA 125 level >40 UI/ml (83%). Pts received a median of 6 courses (1-9). Hematologic toxicity was NCI grade 3-4 neutropenia (54% of cycles), anemia (14%) thrombocytopenia (2%). Febrile neutropenia occurred in 6%. G-CSF, red blood cell and platelet transfusions respectively were required in 20%, 5% and 1%. Dose reduction and course delay were observed in 8% and 15%, mainly due to hematological toxicity. Non-hematological toxicity was moderate including alopecia (83%), grade 3 fatigue (20%), grade 2-4 nausea/vomiting (20%), grade 2 and 3 neuropathy (10 and 3%). The overall rate is 40% (14/34) including 6 pts (18%) achieving complete clinical remission. Stable disease was observed in 6 pts. Response rate is 22% in pts relapsing within 6 months (2/9) and 48% in platinum-sensitive disease (12/25). Median progression-free survival and overall are respectively 9 and 22 months for responders, 7 and 19 months for pts with stable disease, 3 and 6 months for pts with progressive disease.

**Conclusion:** the combination of T and P is feasible and tolerable in outpatient treatment of recurrent AOC and achieves an impressive activity in patients who had received a prior platinum-based regimen without a taxane.

1203 POSTER

## Toxicity-adapted dosing of topotecan in non-taxane-pre-treated, recurrent ovarian cancinoma

A. Mueller[1], G. von Minckwitz[1], T. Einzmann[2], M. Zimmer[3], J. Rudzinski[4], M. Nehmzow[5], S.D. Costa[1], M. Kaufmann[1]. *[1] University Hospital, Gynecology and Ostetrics, Frankfurt, Germany; [2] University Hospital, Gynecology, Freiburg, Germany; [3] Marienhospital, Gynecology, Stuttgart, Germany; [4] Klinikum Schwedt, Gynecology, Schwedt, Germany; [5] University Hospital, Gynecology, Greifswald, Germany*

**Purpose:** A toxicity-adapted schedule of the topoisomerase I inhibitor Topotecan was evaluated in a non-randomised, multi-center, phase II study. Women with epithelial ovarian cancer which relapsed after a prior non-taxane containing chemotherapy were analysed with regard to safety, toxicity and efficacy.

**Patients and Methods:** Including criteria were a recurrent ovarian cancer, no previous taxane treatment, bidimensionally measurable disease, ECOG-performance status of 2 or less, sufficient bone marrow, liver and renal function. Topotecan was administered in the first cycle as a 30-minute infusion with 1.25mg/m2 for 5 consecutive days and was repeated every 21 days. Topotecan dose was adapted dependent on the maximal haematological toxicity after the first cycle to 1.5mg/m2, to 1.0mg/m2, or continued at 1.25mg/m2. No prophylactic use of granulocyte colony stimulating factor (G-CSF) was allowed.

**Results:** 26 patients were recruited into the study. 25 patients were evaluated for toxicity and 23 for efficacy. 18 patients (78%) had one previous chemotherapy, four patients (17%) underwent two and one patient five prior regimens. A planned dose reduction to 1.0mg/m2 was done in 6 patients, whereas an increase to 1.5mg/m2 was possible in 8 patients. After dose-adaptation grade 3/4 leucopenia occurred after the 1st cycle in the 1.0mg/m2 group in 44%. In the 1.5mg/m* group a leucopenia occurred after the 1st cyclein 18%. Thrombopenia occurred only in the first cycle with 24%. Non-haematological side-effects were generally mild, one a grade 4 stomatitis along with a grade 3 pain and infection. The overall response rate was 30,4%. For the dose-reduced group, the dose-increased group, and the initial-dose group the response rate was 50%, 28.6%, and 25%, respectively. Patients who required a dose reduction were treated with a median of 6 (range 3-9) cycles of Topotecan, while both others were treated with a median of 4 (range 2-8 for 1,25mg/m2 and 3-6 for 1,5mg/m2) cycles.

**Conclusion:** Toxicity-adapted dosing of Topotecan maintains efficacy but can reduce toxicity in systemically pre-treated patients with recurrent ovarian carcinoma.