allows for reproducibility of results. We recommend that independent review should be standard in positive phase II & III studies.

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A phase II study of primary intraperitoneal paclitaxel combined with CBDCA/cytoxan (CC) in primary OC

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Methods: Twenty pts with primary stage III ovarian cancer (OC) received intraperitoneal Paclitaxel (PCL) and IV Carboplatin/Cyclophosphamide (PCC). Pharmacokinetic studies were done on IV and IP PCL levels by HPLC. GI toxicity was tolerable: Grade III abdominal pain in one, nausea and vomiting (N/V) Grade III in 15%. Leucopenia WHO Grade III and IV was 75% for PCC without infections. Thrombocytopenia Grade III and IV was 15% without bleeding episodes. Pharmacokinetics: Median plasma $T_{1/2}$ was 9.1 h (range 6.5–13 h). The IP-PCL levels decayed slowly after instillation. The C_{max} IP/IV ratio ranged from 780–1255.

Conclusions: IP-PCL mimics a 24 hrs IV infusion, reaching high drug levels in the peritoneal cavity. Combination with full-dose CC is feasible.

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Topotecan: A "compassionate use" study in patients with advanced epithelial ovarian cancer refractory to other therapies

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Purpose: To evaluate safety and efficacy of i.v. Topotecan in patients with advanced epithelial ovarian cancer with very poor prognosis refractory to other therapies.

Method: 1.25 mg/m^2 Topotecan was given i.v. on five consecutive days, cycle repetition every 3 weeks. Patients must have received two or more prior chemotherapies containing platin derivates and/or paclitaxel. The study focused on safety with efficacy analysis performed in patients with indicator lesions.

Results: The analysis included 109 patients from Germany, UK and Austria, 24 are still ongoing. 108 patients were evaluable for safety and 83 for efficacy. The median age was 56 (range 24–79). 25% of the patients had a performance status >1. Patients had up to 7 previous chemotherapie regimens with a median of 3. Fortynine % of patients received 4 or more courses of topotecan (range 1–12) with a total of 406 courses. In 10% of patients partial response and in 36% stable disease were observed. Time to progression was 13 weeks (10–30), in the range of previously reported results. Serious Adverse Experiences related to topotecan (17/56) were all based on myelosupressive activity, particularly neutropenia.

Conclusion: Topotecan proved to be efficacious in this heavily pretreated patient group with managable myelo- and little nonhematological toxicity.

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Pooled analysis of patients (PTS) treated with topotecan (T) after progression or failure on platinum (PLAT) and paclitaxel (P)

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Purpose: T is a new agent for the treatment of women with recurrent ovarian cancer (ROC) after failure of initial or subsequent chemotherapy. We performed an analysis of pooled data from two multicenter studies in which 200 pts received T after progressing or failing first-line (62 pts) or second-line (138 pts) therapies which included Plat and P.

Methods: T was administered as a 30-min infusion at an initial dose of 1.5 mg/m^2 daily times 5 q 21 days. Responses were confirmed by independent radiological review. Data presented are for the intent-to-treat population.

Results: A total of 1124 courses (crs) were administered (median 4/pt; range: 1–27). Mean age was 56.8 y (range: 20–82 y). Median performance status was 1 (range: 0–3). The response rate was 13.5% (95% CI 8.8–18.2%; 1 CR, 26 PR). Median time to response was 11 wks (range: 3–32 wks). Median duration of response was 24 wks (range: 12–70 wks). Median time to progression was 11 wks (range: 0.7–83 wks). Median survival was 45 wks (range: 1.3–126 wks). One year survival was 42%. Hematologic toxicity was reversible, non-cumulative, and generally not associated with significant sequelae. Gr 4 neutropenia was reported in 82% of crs, with infection or gr 2 fever in 4% of crs. Gr 4 thrombocytopenia and gr 3–4 anemia occurred in 9% and 17% of crs, respectively. Non-hematologic toxicities were generally mild.

Conclusion: Topotecan is a valuable new agent with a manageable toxicity profile in pts with ROC who relapsed after first- or second-line Plat and P. (Supported by SmithKline Beecham.)

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A phase II study of topotecan given as a continuous 21-day infusion every 28 days in platinum pre-treated ovarian carcinoma

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Purpose: Topotecan (TOP) has proven activity in second-line ovarian cancer (OC) when given at 1.5 mg/m^2/d × 5 as a 30 minute infusion q 21 days (d). The aim of this study was to evaluate the efficacy of TOP given by continuous infusion.

Methods: TOP 0.4 mg/m^2/d was given as a continuous 21-d intravenous infusion every 28 d in patients (pts) with advanced epithelial OC.Dose escalation or reduction was permitted and patients could remain on treatment until disease progression. All responses were confirmed by independent radiological review.

Results: 19 pts were recruited and 78 courses (cse) were given (1–10 courses per pt), 2 pts escalated TOP to 0.5 mg/m^2/d and no patient required a dosage reduction. All pts had relapsed after platinum based therapy. 2pts (10.5%) responded and 3 patients (15.8%) had stable disease. One of the responders had refractory disease (progressed on first line carboplatin) and the other had relapsed after a platinum free interval of 26 weeks (wks). In the 2 responding pts response duration was 39.1 and 16 wks. Survival in both pts was >45 wks. Haematological toxicities were reversible, non-cumulative and manageable. Grade 3/4 neutropenia, thrombocytopenia and anaemia were seen in 33/78, 13/78 and 30/78 of cse respectively. Growth factor support was not required but 11 pts in 24 cse required red blood cell transfusion and 1 pt in 1 course required a platelet transfusion. Non-haematological toxicities were generally mild and included nausea, fatigue, diarrhoea and alopecia.

Conclusion: Topotecan given by 21-day infusion has activity in ovarian cancer.

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Activity of Gemcitabine in stage 3 or 4 ovarian cancer: Patients previously treated with cisplatin (CP)-containing regimens

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Purpose: GEMZAR® (Gemcitabine, GEM) is a nucleoside analogue active against a variety of solid tumours. In a phase II study a 19% response rate was observed in 42 evaluable and CP-resistant ovarian cancers (Lund et al. JNCI, 1994; 86: 1530–1533).

Methods: From December 93 to March 95, we investigated the efficacy and the safety profile of GEM in stage 3 or 4 ovarian cancer. Major inclusion criteria were: previous CP-containing regimens, measurable disease, adequate renal, hepatic and bone marrow functions. GEM (1200 mg/m^2) was administered as a 30 min infusion on days 1, 8, 15 of a 28 day cycle.

Results: 38 pts were enrolled. Mean age was 58 years, median Karnofsky Score was 90 (60–100), FIGO stage at entry was 3 for 13 pts, 4 for 25 pts. 4 pts were ineligible (1 pt for diagnosis not confirmed and 3 pts for insufficient therapy) and 2 pts were lost to follow-up before evaluation. With