and dose distribution was evaluated and compared to that of a standard cervical applicator and CT based planning.

**Results:** The specially designed adjustable cervical applicator prevented overdosage of the organs at risk and undertreatment of the distant tumor spread in all cases. With no hazard of a possible radiation, or mechanical injury the radiation doses could be increased without increasing the possibility of acute or late complications rate. Local tumor control was excellent in 12 patients (75%), moderate in 3 cases (18%) and poor in 1 patient (6%). The treatment was well tolerated by the patients. Unlike other adjustable intraluminal applicators due to the thin diameter of the catheter, the insertion of the applicator was possible without the need of previous dilatation and was fixed by a surgical suture for the whole period of the treatment.

**Conclusion:** The used MR compatible, flexible applicator allows safe and reproducible cervical radiotherapy with no added discomfort or hazard for the patient. The technique is suitable for other intraluminal applications, too, such as the treatment of malignant airway obstructions, bile ducts, pancreatic duct, ureter and the vascular system.

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## Early results of a phase II study of oral topotecan and intravenous cisplatin in epithelial ovarian cancer recurring more than 6 months following initial platinum therapy

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**Background:** Combination chemotherapy is being evaluated for recurrent platinum sensitive epithelial ovarian cancer. In-vitro studies suggest synergy between topotecan (TOP) and cisplatin (CDDP). This combination administered intravenously has been shown to have activity in epithelial ovarian cancer and is being evaluated as part of first line therapy. The oral formulation of TOP has been trialed as single agent therapy in recurrent ovarian cancer. It appears to possess similar efficacy to intravenous TOP and has the advantage of convenience of administration. We report the preliminary results of a Phase II clinical trial of oral TOP in combination with IV CDDP in patients with late recurrence of epithelial ovarian cancer.

**Materials and Methods:** Patients with ovarian cancer relapsed >6 mo following initial platinum therapy and with measurable disease were treated with oral TOP (1.25 mg/m$^2$) administered daily for 5 consecutive days every 21 days plus IV CDDP (50 mg/m$^2$) being administered on day 1 of each 21-day course. Colony Stimulating Factor support was allowed during therapy.

**Results:** To date 30 eligible pts have been enrolled. Preliminary data is available on 20 pts. The median age was 54 (range = 42 to 70) with a PS of 0 (8pts) or 1 (12pts). Median follow-up is 63.5 weeks (range = 15.9 to 109.3). Out of 16 pts whose response results were available there were 8 responders (50%) including 2 CR (12.5%) and 6 PR (37.5%). An additional 4 pts (25%) completed treatment with stable disease. The median time to disease progression was 36.7 weeks (95%CI=19.3 to 40.3). Median survival has not yet been reached. Toxicity data has not currently been fully analysed but generally has been predictable. Available haematological toxicity reports 6/20 (30%) grade 3 and 12/20 (60%) grade 4 neutropenia, 4/20 (20%) grade 3 and 4/20 (20%) grade 4 thrombocytopenia, and 6/20 (30%) and 1/20 (5%) grade 3 and 4 anaemia respectively. Updated results on toxicity and efficacy will be presented at the meeting.

**Conclusion:** Oral TOP with IV CDDP in platinum sensitive relapsed ovarian cancer has activity that compares favourably with the same combination given intravenously.

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## Clinical significance of beta catenin immunoexpression in epithelial ovarian cancer

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**Backround:** Beta catenin plays a dual role in the cell: it is a component of the E-cadherin-catenin complex, linking the cytoplasmic domain of cadherin to the actin cytoskeleton of the cell and plays a role in the Wnt signaling transduction pathway.

**Aim:** To determine the biological and clinicalpathological relevance of beta catenin immunoexpression pattern in ovarian cancer and determine its relationship with patient survival.

**Materials and Methods:** Beta catenin was immunohistochemically evaluated in formalin-fixed, paraffin embedded samples of 104 patients with primary ovarian carcinomas.

**Results:** In 104 carcinomas, beta catenin immunoreactivity was negative in 15 (14%) cases, and present in 89 (86%) cases. Absence of beta catenin immunoexpression correlated with the serous and clear cell histological subtypes (p=0.026). Negative immunoreactivity for beta catenin significantly predicted poorer overall survival as compared with the membranous expression of beta catenin in both univariate (P=0.022) and multivariate analyses (P=0.0039). The presence of residual tumour also predicted poorer overall survival in both univariate (P<0.001) and multivariate analyses (P=0.0340).

**Conclusion:** The presence of residual tumour as well as the negative immunoexpression of beta catenin seems to be a useful marker in selecting patients with ovarian carcinomas likely to run a less favourable course. In the future, a large prospective study will need to be performed to determine whether the expression of beta catenin can provide important evidence on which to base therapeutic strategies.

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## The role of 3rd therapy in recurrent ovarian carcinoma or primary peritoneal carcinoma

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**Objectives:** 3rd line chemotherapy is routinely applied for recurrent ovarian carcinoma. However, its role is unclear. We retrospectively evaluate our experience with this approach.

**Methods:** From January 1990 to December 1999, we registered 615 pt's with ovarian or primary peritoneal carcinomas. Of them, 49 (7.9%) received at least 3 different chemotherapeutic treatments. CA 125 response is presented according to Rustin criteria. Survival and time to progression times were calculated with Kaplan-Meier curve using Epistat 5.0.

**Results:** Median age was 59 (36-78) years, median P.S 1 (0-2). Forty one (83.7%) Pt's had ovarian carcinoma and 8 (16.3%) pt's had primary peritoneal carcinoma. Optimal debulking was possible in 31 (68.8%) pt's. Median CA 125 level was 108 (4-4244) IU/ml. First therapy defined 29 (59.1%) pt's as cisplatin sensitive. Second therapy included taxanes/platinum-based regimen in 14 (28.5%), platinum-based in 33 (67.3%) pt's paclitaxel/5-FU in a single pt. Third therapy was initiated a median of 27.1 (7.2-85) months from diagnosis. It included topotecan in 14 (28.5%) pt's, taxanes-based in 16 (32.6%) pt's, platinum-based in 5 (10.2%) pt's, 5-FU/leokoverine or gemcitabine each in 3 (6.1%) and various single agents in 8 (16.3%). CA 125 50% response occurred in 13 (26.5%) pt's (95% CI, 14.9%-41%). CA 125 75% response was noted in 6 (12.2%) pt's, while CA 125 stabilization occurred in 20 (40.8%) pt's. Median time to progression was 4.2 (0.7-48.5) months, longer in the CA 125 responders (7.2 vs 3.4 months, P=0.034). The median survival of all the Pt's was 16.7 (2.1-116.5+) months, longer in CA 125 responders (29.5 vs 12 months, P=0.02). It was not statistically affected by initial optimal debulking, or primary cisplatin sensitivity. Subsequent treatments were delivered as the following: 4th- 39 (79.5%) pt's, 5th- 22 (44.8%) pt's, 6th- 12 (24.4%), 7th- 2 (4%) pt's 8th and 9th in single pt's.

**Conclusions:** 3rd line therapy is active in selected pt's with recurrent ovarian carcinoma. These Pt's may enjoy prolonged survival which is not affected by initial optimal debulked state or cisplatin-sensitive disease.

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## Determining predominating histologic component in malignant mixed mullerian tumors: does it really work?

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**Background:** Malignant mixed mullerian tumors (MMMT) are aggressive tumors, usually diagnosed in advanced stage. Cases of MMMT derive from either ovary or uterus. In our study, we investigated the role of carcinomatous and sarcomatous component on response to chemotherapy and on disease outcome.

**Methods:** We retrospectively analyzed 17 patients with MMMT who were treated in our outpatient clinic from 1998 to 2003. All the parraffin specimens were revealuated according to the histopathologic features (primary site and percentages of carcinomatous and sarcomatous component) and the effect of dominant histologic type on response to treatment.