(p=0.033). A correlation was also found between the post-CT-RT positive MIBI and CR (p=0.030).

Conclusion: This preliminary report showed that pre-CT-RT MIBI, Ki-67, and p53 were not predictive for response to CT-RT, but the post-CT-RT MIBI and the decrease of uptake were correlated with the response. Pre-CT-RT MIBI was also correlated with low expression of mutated p53. These data suggest that changes of MIBI uptake after CT-RT can be related to the response to treatment.

Gynaecological cancer

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Overall survival advantage for pegylated liposomal doxorubicin compared to topotecan in recurrent epithelial ovarian cancer

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Background: A recent phase III study compared the efficacy and safety of pegylated liposomal doxorubicin (Doxil®/Caelyx®) with topotecan in patients with recurrent epithelial ovarian cancer that recurred after or did not respond to first-line, platinum-based chemotherapy (Gordon, et al. *J Clin Oncol.* 2001;19:3312-3322). Response rates were found to be similar for both treatment groups. Final survival data from this study are now reported.

Material and Methods: Patients (N = 474) were randomly assigned (1:1 ratio) to treatment with pegylated liposomal doxorubicin 50 mg/m^2 every 28 days or topotecan 1.5 mg/m^2/day for 5 consecutive days every 21 days. Patients were stratified prospectively based on whether they had platinum-sensitive/refractory disease and the presence/absence of bulky disease. Primary efficacy endpoints were progression-free and overall survival.

Results: Overall survival was longer in patients treated with pegylated liposomal doxorubicin compared to those treated with topotecan (median 63 and 60 weeks, respectively; P = 0.05, HR = 0.82 [0.68, 1.00]). In the subset of patients with platinum-sensitive disease (46%), this survival advantage was even more striking for patients treated with pegylated liposomal doxorubicin compared to topotecan (median 112 and 77 weeks, respectively; P = 0.002, HR = 0.63 [0.47, 0.85]). In the subset with platinum-refractory disease, survival was similar in the 2 treatment groups (median 36 and 41 weeks, respectively; HR = 1.01 [0.78, 1.31]). As of December 2002, 29 patients initially treated with pegylated liposomal doxorubicin and 10 topotecan-treated patients remain alive. A more favorable toxicity profile was reported with pegylated liposomal doxorubicin, as patients experienced fewer severe adverse events and required less hematologic support and significantly fewer dose modifications.

Conclusions: Patients treated with pegylated liposomal doxorubicin had longer overall survival compared to topotecan-treated patients. The overall survival advantage was more than 35 weeks in patients with platinum-sensitive disease treated with pegylated liposomal doxorubicin. To date, this is the only head-to-head study demonstrating a survival advantage in recurrent epithelial ovarian cancer.

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Phase I dose finding study of capecitabine, cisplatin and radiotherapy in the treatment of locally advanced squamous cervical cancer

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Background Materials and methods 13 patients with Stage II (7) or Stage III (6) received pelvic radiotherapy (45Gy in 25f) plus a selectron intra-uterine insertion (median A point dose 26.00Gy at 1.53Gy/hr). All but one patient (4 cycles only) received 6 weekly cycles of cisplatin (40mg/m^2). It was planned to give daily capecitabine for 42 days to cohorts of 6 patients using escalating doses. The MTD was defined as 2 patients experiencing Grade(G) 3 toxicity in any one cohort. The starting dose level was 600mg/m^2 BD and the second 900mg/m^2/BD

Results Capecitabine dosage 6/6 patients in cohort 1 and 5/7 in cohort 2 received capecitabine at or very close to the protocol dose. Capecitabine was discontinued after 27 days in 1 patient in cohort 2 because of Grade 3 diarrhoea, febrile neutropenia and thrombocytopenia. 1 patient in cohort 2 had difficulty swallowing the tablets, discontinued treatment after 4 days and was replaced. Two patients in cohort 2 experienced G3 toxicity (diarrhoea and febrile neutropenia).

Survival 4 patients have died. The actuarial progression free survival at 12 months is 64% (se = 15%)with a 15 month survival of 55% (se = 17%).

Acute toxicity 1 patient in cohort 1 developed G 3 diarrhoea. 2 patients in cohort 2 developed febrile neutropenia and 1 of these also had G 3 diarrhoea.

Late Toxicity 2 patients (1 from each cohort) developed RTOG/EORTC G 3 late toxicity (bladder and vaginal mucosa respectively) at 9 and 15 months after treatment.

Conclusion The MTD of capecitabine given with pelvic irradiation and weekly cisplatin was found to be 900mg/m^2/BD. The recommended dose level of capecitabine in this combination is 600mg/m^2/BD.

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Phase II study of OSI-774 given in combination with carboplatin in patients (pts) with recurrent epithelial ovarian cancer (EOC): NCIC ctg Ind.149.

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Background: Response rate to carboplatin in pts with recurrent EOC is proportional to the progression free period after completion of first-line platinum-chemotherapy. Pts relapsing within 6 months are considered platinum resistant (PR), and pts relapsing after 6 months, sensitive (PS). OSI-774 is an orally active, potent, selective inhibitor of EGFR tyrosine kinase inhibitor with single agent activity in ovarian cancer (Finkler et al P ASCO Abstract 831, 2001). EGFR inhibitors may potentiate the antitumour effects of cytotoxic agents, and may beneficially modulate drug resistance.

Methods: Pts with relapsed EOC, measurable disease, and $\leq$ 2 prior chemotherapy regimens (the first regimen must have contained platinum) were entered into one of 2 strata: PR or PS. Both strata have 2-stage designs, with sample sizes of 30 pts (15: 15) and 15 pts (8:7) respectively. Carboplatin was given at AUC 5 IV q 21days with OSI-774 150mg day.

Results: 34 pts have been accrued to date. Acneiform rash, fatigue, diarrhea, nausea and dry skin were the most common toxicities. 2 pts had carboplatin hypersensitivity allergic reactions. No grade 4 hematologic toxicity occurred. 18 PS pts were accrued in 2 stages; preliminary response data suggest 10 of 16 currently evaluable pts have achieved as yet unconfirmed objective responses. 16 PR pts have been accrued in stage 1. Response data are as yet immature.

Conclusion: OSI-774 can be administered in combination with carboplatin at a dose of AUC 5. The combination has activity in PS patients; mature response data on both PR and PS strata will be updated.

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Patterns of relapse influenced by hematogenous tumor cell dissemination in patients with cervical carcinoma of the uterus

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The presence of isolated tumor cells (ITC) in the bone marrow at the time of primary diagnosis has been found to indicate an increased risk for subsequent development of distant metastases in various solid tumors. This study evaluates the prevalence and prognostic significance of ITC in patients with primary carcinoma of the cervix uteri.

We immunocytochemically analyzed bone marrow aspirates of 130 patients with newly diagnosed carcinoma of the cervix uteri for the presence of cytokeratin(CK)-positive cells from May 1994 until January 2001. We used a quantitative immunoassay with the monoclonal anti-CK antibody A45-B/B3 and evaluated 2 x10^6 bone marrow cells per patient. Patients were followed prospectively for a median of 43 (range, 1-85) months.

ITC were found in the bone marrow of 38 patients (29%). The presence of ITC did not correlate with the FIGO tumor stage (P = 0.61), pelvic and paraaortal lymph node involvement (P= 0.41), nor with histopathological grading (P= 0.67), the histological type of the carcinoma (P= 0.93), invasion of lymph (P=. 93) and blood vessel (P= 0.92), or menopausal status (P= 0.17). The bone marrow status at the time of primary diagnosis did not correlate with the overall survival as estimated by Kaplan-Meier-Analysis (P= 0.30). However, distant metastases occurred in 5% of the patients (n=5) with negative and in 15% of the patients (n=6) with positive bone