Five patients (3 with cCR and 2 with cPR, all stage IIb) underwent hysterosalpigophorectomy after the end of the treatment. The three cCR and the two cPR have been confirmed histologically. Six out of 21 patients presented toxicity Grade 3-4: mucositis (3), haematologic toxicity (2) and dermatitis (1). No toxic death has been noted.

Conclusion: The combination of standard fractionated RT with concurrent administration of CPT-11, IFNa2b and amifostine is a highly active and well tolerated treatment for LACC.

181 POSTER

A pilot phase II study of cisplatin and capecitabine in patients with recurrent cervical carcinoma

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Background Platinum is the mainstay of treatment in advanced or recurrent cervical carcinoma, however, the duration of response is short lived as well as the median survival. Fluorouracil (5-FU) has been shown to be active in cervical carcinoma. Capecitabine, an oral fluoropyrimidine carbamate, is sequentially converted to 5-FU by thymidine phosphorylase (TP) which is found at higher concentrations in cervical carcinoma than normal tissue. In addition, cisplatin further upregulates TP. Capecitabine plus cisplatin has the potential to be an active treatment, which is more convenient than 5-FU-cisplatin.

Materials and methods This study combines capecitabine and platinum in patients with recurrent cervical carcinoma with no potentially curative standard treatments. Fourteen patients (12 squamous cell carcinoma, and 2 adenocarcinoma) with a median disease-free interval of 11 months (range 2-96) received cisplatin 50 mg/m^2 intravenously on day 1 and oral capecitabine 1000 mg/m^2 twice daily for two weeks with a one week rest period.

Results Median age was 54 years (range, 33-74). A total of 77 cycles were administered with a mean of 5.5 cycles (range, 3-6) per patient. Four of the fourteen patients had complete response (28%), 4 had partial response (28%), and 3 had disease stabilization (21%). The median follow-up time was 15 months (range, 6-48) and median time to progression was 14 months. There were grades III to IV neutropenia, palmar-plantar erythrodysesthesia (PPE), and mucositis in 13%, 4%, 3% of the cycles, respectively.

Conclusion This active yet convenient combination of capecitabine and cisplatin shows a high response rate, long time to progression and acceptable toxicities. Further clinical exploration of the present combination appears warranted.

182 POSTER

The clinical implications of radiotherapy on renal function in patients with hydronephrosis in stage IIIB cancer of the cervix

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Background: Acute urinary obstruction is a life-threatening complication in this group and often produces a break in radiation treatment, which adversely affects outcome. The ability to predict which patients are more likely to require ureteral stenting would allow the clinician to arrange elective stenting prior to radiation treatment, thus avoiding a break in treatment.

Materials and Methods: Renal imaging, renal function and creatinine clearance were analysed for all stage IIIB patients undergoing radical chemo/radiotherapy at our institution from Jan 2000 to Jan 2002. Co-morbid conditions and intercurrent medications likely to adversely affect renal function were noted. Details of stenting procedures were obtained.

Results: Risk factors associated with ureteral stenting in Stage IIIB cervical cancer were; a) medication, 10% gentamicin usage, 70% NSAID usage, b) comorbid conditions, urinary tract infection 30%, hypertension 10%, smoker 90%. 27% did not require urinary diversion and all of these had mild unilateral hydronephrosis. 18% of patients had stents placed at presentation (prior to radiotherapy) and of these 67% had bilateral hydronephrosis. 37% of patients required stenting during radiotherapy and all had severe bilateral hydronephrosis. This meant a break in radiation treatment of, on average one week. 18% required urinary diversion after radiotherapy. The average creatinine clearance was 70mls/min in the unilateral hydronephrosis group and 45mls/min in the bilateral hydronephrosis group. In those with no urinary diversion the average creatinine clearance was 80mls/min, in those stented at presentation 62mls/min and those requiring urinary diversion during radiotherapy had the lowest average creatinine clearance at 28 mls/min.

Conclusions: Patients with Stage IIIB cancer of the cervix with bilateral hydronephrosis are more likely to have a low creatinine clearance. There is a trend for those with moderate to severe bilateral hydronephrosis at presentation and a low creatinine clearance to be much more likely to require urinary diversion during radiotherapy. The 37% of patients requiring urinary diversion during radiation had a break in treatment of on average one week. These patients have a combination of bilateral hydronephrosis and low creatinine clearance and should be considered for elective urinary diversion prior to radiation treatment.

183 POSTER

Intensity modulated arc therapy and carboplatin/paclitaxel chemotherapy for treatment of high-risk endometrial malignancies

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Background: Whole pelvic IMRT is complex, requiring multiple fields, often with field splitting and junction problems. We developed an Intensity Modulated Arc Therapy (IMAT) radiation technique that simplifies treatment planning and delivery.

Materials and Methods: Five women with high-risk carcinoma of the endometrium received 4-6 cycles of paclitaxel and carboplatin sequentially with radiotherapy. Using axial CT slices, the tumor bed, iliac and pre-sacral vessels, ± lower para-aortic region were contoured as GTV. A CTV with 5-10 mm margin and PTV with 7 mm margin were generated. The small bowel, iliac crests, femoral heads, bladder and rectum were contoured as critical organs. Balancing the complexity of the arc technique with normal organ sparing, two anterior intensity modulated arcs, from 300° to 30° (IEC convention) and 330° to 60° were used. DVH, dose distribution, dynamic MLC patterns, and comparisons to conventional treatment and 5-field IMRT inverse plans were generated.

Results: Using the IMAT, 95% of the tumor volume received dose above 45 Gy, the nodes 40-45 Gy and bladder/ rectum $\leq$ 45Gy. This technique allowed sparing of the small bowel, iliac crests and femoral heads. The dose to the iliac crests was reduced compared to conventional radiation therapy and similar to IMRT. The volume of small bowel receiving dose above 45Gy was 80%, 10%, 15% for conventional, IMRT, and IMAT technique respectively. Treatment has been well tolerated with no significant acute toxicities.

Conclusions: IMAT provides an effective technique to treat the tumor bed and regional nodes while allowing a conformal avoidance of the bone marrow and small bowel compared with conventional radiation therapy. While critical structure sparing is similar to multi-field IMRT, our method is simpler to plan and deliver and was well tolerated. Ongoing work will assess both the clinical outcome and long term toxicity of this multi-modality treatment strategy.

184 POSTER

Improved dose distribution for complex radiotherapy of cervical cancer using an innovative brachytherapy technique.

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Purpose: The aim of this paper is to introduce a technique for cervical, MR based 3D planned high dose rate brachytherapy resulting in improved dose distribution in the GTV as compared to that obtained with commercially available standard cervical applicators.

Materials and methods: Between January 2002 and January 2003, 16 patients received external beam- and brachytherapy as treatment for cervical cancer. In addition to the CT based shrinking volume conformal teletherapy, to avoid excessive doses to the healthy structures during complex cervical radiotherapy a special adjustable applicator was used for the brachytherapy. The applicator is suitable for situating the radioactive source in the axis of the treated uterus. Isodose curves were calculated upon the information of the MR image with the catheter at the treatment site

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.

185 POSTER

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.

187 POSTER

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.