of at least six cycles of carboplatin (AUC 5) and docetaxel 75 mg/m^2 d1q22. Hemoglobin levels were obtained before each cycle of the therapy. Study objectives were response, time-to-progression and overall-survival (OAS). Univariate analysis and cox-regression studies were undertaken to evaluate the prognostic impact of the hemoglobin level before und during chemotherapy.
Results: Median age of the patients was 57 years. The majority of the patients was diagnosed at stage III ovarian cancer and had received best cytoredutive surgery. 415 cycles of four different carboplatin-based chemotherapy regimen were administered (Mean 6, range 3–20). Mean hemoglobin level before therapy was 11.5 g/dl, during therapy 11.2 g/dl and after therapy 10.8 g/dl. In cox-regression analysis hemoglobin levels before and during chemotherapy showed a prognostic relevance in terms of time-to-progression ($p < 0.01$). In addition, univariate analysis revealed a statistical trend for hemoglobin levels before ($p = 0.09$) and during ($p = 0.06$) chemotherapy to have prognostic relevance in terms of time-to-progression.
Conclusions: The pretherapeutic hemoglobin level seems to have prognostic relevance for patients with primary ovarian cancer undergoing carboplatin-based chemotherapy. Though the majority of these patients is diagnosed in advanced tumor stages the therapeutic intention is curative. For that reason further prospective trials should be undertaken to prove the prognostic impact of hemoglobin levels before and during chemotherapy. Based on these data the role of anemia correction as standard supportive therapy should be discussed in the treatment of patients with primary ovarian cancer.

937 POSTER

Analysis of predictors of toxicity in patients with stage III endometrial cancer confined to the pelvis treated with external-beam radiotherapy

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Purpose: Patients with stage III endometrial cancer often receive pelvic radiotherapy (RT). This study assesses predictors of acute and late adverse events in these patients.
Methods: Records of 121 patients with pathologic stage III endometrial adenocarcinoma treated between 1990 and 2003 were reviewed. External beam RT was delivered to 66 patients with a median dose of 45 Gy in 25 fractions. Fifty patients (76%) also received high-dose-rate brachytherapy as a boost, typically 6 Gy in one session. Adjuvant chemotherapy (CT) was delivered to 8 patients (12%). The influence of age, body mass index (BMI), history of smoking, diabetes, hypertension, inflammatory bowel disease, previous bowel obstruction, previous abdominal and pelvic surgery, radiation dose, beam energy, field arrangement and size, and treatment with CT was evaluated as potential predictors of toxicity.
Results: The median follow-up is 39 months. Five-year overall survival is significantly improved in patients treated with adjuvant RT (68%) compared to those with resection alone (50%; $p = 0.029$). Five-year disease-free survival in patients treated with or without RT was 67% and 37%, respectively ($p = 0.004$). Acute and late lower GI and GU toxicities are shown in the table. Only grade 1 or 2 upper GI toxicities were seen in 8% of patients. Treatment with CT was found to significantly correlate with the acute upper GI toxicity. Acute lower GI toxicity significantly correlated with BMI and number of radiation fields. Acute GU toxicity significantly correlated with history of pelvic surgery. In addition, there was a trend for correlation between acute GU toxicity and beam energy ($p = 0.069$). Treatment with CT significantly correlated with the development of hematological toxicity, although grade 2 or higher adverse events was not observed. Late GI toxicity was found to significantly correlate with history of small bowel obstruction, previous pelvic surgery, and number of radiation fields. No treatment-related deaths were observed.
Conclusions: Radiotherapy improves survival in patients with stage III endometrial cancer confined to the pelvis and is well-tolerated. Patients with higher risk for developing late complications were identified. Advanced techniques, such as intensity-modulated radiotherapy, may be beneficial in the treatment of these selected patients.

Grade	Acute		Late	
	Lower GI	GU	Lower GI	GU
1	14 (21%)	11 (17%)	6 (9%)	2 (3%)
2	32 (48%)	3 (5%)	3 (5%)	0 (0%)
3	1 (2%)	2 (3%)	0 (0%)	0 (0%)
4	1 (2%)	0 (0%)	2 (3%)	0 (0%)

938 POSTER

A biweekly schedule of pegylated liposomal doxorubicin (C), can it reduce the skin toxicity? Results of a phase-II study of heavily pre-treated patients with recurrent ovarian cancer

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Background: C is a pegylated liposomal doxorubicin formulation and has been approved for the treatment of recurrent ovarian cancer. Palmar-plantar erythrodysesthesia (PPE) has been reported as being the dose-limiting toxicity and effects patients' quality of life. We conducted this phase-II trial based on the encouraging results of a biweekly schedule of C in patients with AIDS-related Kaposi's sarcoma.
Methods: A multi-institutional phase-II study was performed to analyze the toxicity profile of PLD (20 mg/m^2/q 14d) in heavily pre-treated patients with ROC. Eligibility criteria: ROC, prior treatment with Platinum and Taxan. Statistic: 2-Step-Design, in case of a positive first step ($n = 26$): > 2 response+<6 events of PPE (CTC Grade III/IV), a total number of 60 patients must be recruited; power: 80%, $p < 0.05$, based on a 10% reduction of PPE (95%CI). Eligibility criteria: relapsed epithelial ovarian cancer, prior treatment with platinum- and paclitaxel-containing chemotherapy, ECOG status 0–2, organ function (e.g. cardiac, liver) within normal range, written informed consent.
Results: A total of 64 patients were recruited (10/2001–02/2004). 553 courses (median: 7, range: 1–35) were evaluable. Median age was 59 (38–81). Patients were generally heavily pretreated: Only 13 patients has been in second-line, most of the patients were in third- or fourth-line. Ten patients were in fifth-line. Overall, the treatment was well tolerated. 30 patients developed skin toxicities: 18 patients with grade I, 9 with grade II and only 3 patients with grade III. These side effects occurred after a median of 5 courses. Haematological toxicity profile was unincisive: only in three patients anaemia grade III and in one patient thrombocytopenia grade III was observed. Clinical response were evaluable by CA-125-monitoring and radiological measurements. Two patients achieved complete response, further five patients partial response and 13 stable diseases as best response criteria. The progression-free survival for these heavily pre-treated patients was median 6.4 months. The overall survival was median 13.4 months.
Conclusion: These results of heavily pre-treated patients shows, that the biweekly schedule of C is effective, secure and well tolerated, with a low incident of skin toxicity.
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939 POSTER

Management of sarcomas of female genital tract

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Aim: Sarcomas of the female genital tract are presented with poor clinical picture and a wide spectrum of histological findings. Only a third of patients go for surgery with an established diagnosis. Currently, the main method of treatment of sarcomas of the female genital tract is surgery. The efficacy of chemotherapy and radiotherapy are questionable. Surgery remains the main mode of treatment. So, the aim of our study is to establish the optimal treatment modalities for these tumors.
Methods: 406 patients treated at the NNBRCRC from 1970 to 2002 were retrospectively analized: 168 patients with leiomyosarcoma, 88 – endometrial stromal sarcoma, 113 – carcinosarcoma, 34 – rabdomyosarcoma, 2 – adenosarcoma, 1 – liposarcoma. All patients were analyzed according to two basic parameters: histological structure and tumor site. Surgical treatment, as independent method, was performed to 189 patients, chemotherapy – 4 patients, radiotherapy – 8 patients. Combined treatment, including surgery and postoperative chemotherapy was performed to 76 patients, surgery+radiotherapy – 60 patients. Complex treatment (surgery+chemotherapy+radiotherapy) was performed to 60 patients.
Results: local recurrences and distant metastases after the initial treatment occurred in 188 patients (46.3%), 80% from them were multiple lesions. Site of the metastases correlated with the histological structure of the sarcoma. Uterine sarcomas (92.2%) are the most common in our material. Sarcoma of the cervix, ovaries, vulva, vagina are rare and compose only 7.8%. Histologically, smooth cell tumors – leiomyosarcomas (41.4%) are the most common. Immunohistochemistry and electronmicroscopy play a major role in establishing the diagnosis. One of the most important prognostic factors of sarcomas of the female genital tract is the morphological structure of the tumor: 5 year overall survival of patients with leiomyosarcoma – 48.3+4.2%; low-grade endometrial stromal sarcoma-85.8+5.3%; high-

grade endometrial stromal sarcoma – 45.1+8.3%; carcinosarcoma – 27.2+6.0%. Sarcomas of the ovaries have extremely poor prognosis.
Conclusion: According to our data, the optimal surgery for leiomyosarcoma is hysterectomy in the reproductive age and hysterectomy with bilateral salpingo oophorectomy in the postmenopausal period; low-grade endometrial stromal sarcomas – radical hysterectomy with bilateral pelvis lymphadenectomy; high-grade endometrial stromal sarcomas – radical hysterectomy with bilateral pelvis lymphadenectomy and omentectomy, due to the high rate of metastasis in retroperitoneal lymph nodes (20%), ovaries (19.6%), great omentum(22%).

940 POSTER

The prognostic significance of volumetric evaluation by magnetic resonance imaging in radiotherapy for patients with cervical cancer

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Background: To investigate the prognostic significance of tumor volume response using MRI for volumetrically assessment for patients with cervical cancer.
Methods and Materials: From March 1997 to August 2002, 54 patients who were treated with radiotherapy for cervical cancer were evaluated. All patients were given external beam radiotherapy over the whole pelvis (median 50.4 Gy) and intracavitary brachytherapy. All patients had taken three serial MR examinations at the start of radiation therapy (pre-RT), at 4 weeks after the start of radiotherapy (mid-RT), and 1 month after treatment completion (post-RT). Tumor volume was calculated by summation of all the areas of tumor and multiplying by the slice profile using T2-weighted images of each MR examination. Follow-up scored from the start of radiation treatment range from 4 to 84 months (median: 42 months).
Results: Mean tumor volumes in MR images at pre-RT, mid-RT and post-RT were 51.3 cc (from 1.1 to 153.1 cc), 13.5 cc (from 0 to 66.0) and 2.2 cc (from 0 to 42.7 cc) respectively. In mid-RT MR images, the number of patients who had complete remission (CR), partial remission and stable disease were 9 (16.7%), 38 (70.4%) and 7 (13.0%) respectively. In post-RT MR images, the number of patients who had CR and non-CR were 39 (72.2%) and 15 (27.8%). The incidence of recurrence was 33.3% (loco-regional failure: 11.1%, distant metastasis: 25.9%). In mid-RT MR images, the incidence of recurrence was 0% in patients with CR compared with 40.0% in those with non-CR (p-value = 0.0218) and the 4-year disease-free survival was 100% and 58.9%, respectively (p-value = 0.0369). In post-MR images, the incidence of recurrence was high in patients with non-CR (53.3%) compared with the patients with CR (25.6%) (p-value = 0.0532) and the 4-year disease-free survival was 53.3% and 69.9% respectively (p-value = 0.0515). The tumor response in mid-MR images affected significantly by clinical staging and initial tumor volumes. According to FIGO stage I, II and III-IV the rates of CR were 57.1%, 11.8% and 7.7% respectively (p-value = 0.0203) and the rates of CR were 38.9% and 5.6% in less than 32 cc and more than 32 cc of initial tumor volume respectively (p-value = 0.0041). In post-MR images, initial tumor volume was only significantly correlated with the tumor response (p-value = 0.0099, less than 32 cc: 94.4%, more than 32 cc: 61.1%).
Conclusion: In clinical practice, the evaluation of the volume response on MR images during radiotherapy may be helpful in determining the radiation dose and the timing of brachytherapy to increase the tumor regression after radiotherapy.

941 POSTER

Late severe complications in advanced cervical cancer treated by concomitant high dose rate brachytherapy and external radiotherapy

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Introducing: Depending on its tradition or infrastructure each center applies different treatment regimens. The aim of this retrospective study was to assess the influence of the treatment regimens on late severe complications in treatment of advanced cervical cancer by concomitant external beam radiotherapy and high dose rate brachytherapy.
Material and methods: A retrospective analysis of 151 patients with FIGO stage IIB-IV carcinoma of the cervix treated by radiotherapy during 1993 and 1995 was done. Radiotherapy for all patients included doses of 46–50 Gy of 6–10MV external fotons to pelvis in 22–24 fractions. Depending of infrastructure a group of 68 patients were treated brachytherapy (BT) with Ir-192 HDR stepping source and 83 patients were treated by Co-60 HDR fixed source. Brachytherapy (dose and volume evaluation Level 1) was delivered in 5 applications and 7 Gy-8 Gy to the point A, to a dose of 35–40Gy. An applicator with two vaginal and one intrauterine source carrier(s) is used. Central shielding was designed after 20 Gy of pelvis irradiation, for a certain doses of external radiotherapy (50 Gy) or for applied BT doses of 40 Gy at the point A.
Results: Late severe complications Grade 3+4 (French-Italian glossary) were determined in 13.2% (20/151pts), G3 11.26% and G4 1.99%, for the follow-up period of 5 years, seen at the rectosigmoid, the bowel and bladder. A correlation of complications with stage of disease and dose including pelvis dose and BT dose was studying. Occurrence of G 3+4 complications was in St. II 10.6% (8/75pts) in St. III 16.9% (11/65pts) in St. IVa 9% (1/11pts). The high percentage of complication 33.3% (5/15pts) was found in a case of dose escalation: external radiotherapy dose of 50 Gy/24f and BT dose of 40 Gy/5f to pint A(with central shielding) and 19.2% (5/26pts) if external dose of 46 Gy/22f and BT dose of 40Gy to point A was given. The acceptable percentage of severe complication 9.1% (10/110pts) was found in most frequent dose schedules: external beam dose of 46Gy/22f and BT dose of 35 Gy/5f to point A.
Conclusion: In high dose rate BT an increase in dose might increases the injury to late – responding tissue at the Level I dose and volume evaluation. Central shielding in a case of increased total given dose, can't reduce the developing of late sever complication. With the sophistication of dose delivery it might be improved treatment planning and this should allow dose escalation with sparing of normal tissue.

942 POSTER

Estimated annual number of Pap III and Pap IV patients and associated resource use in the pre-HPV vaccine era in Germany

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Background: Human Papillomavirus has been implicated in the etiology of cervical neoplasia. Despite recent advances in screening and treatments, cervical cancer remains an important public health problem. The study aim was to assess the resource use associated with the diagnosis and management of patients with Pap III and IV, in the pre-HPV vaccine era in Germany.
Methods: A retrospective multicentre observational study was conducted with 43 gynecologists (79% private; 15% public; 6% both sectors). The study included patients diagnosed with Pap III/IIID or IV/IVa/IVb (N = 99) between February and March 2004.
Resource use: Clinical and resource use data were collected for a maximum period of one year (February 2004–2005). Resources included consultations, medications, interventions, diagnostics and length of hospital stay for Pap III and IV as well as adverse events.
Extrapolation to Germany: The average number of Pap III and IV cases per gynecologist was multiplied by the total number of gynecologists in Germany to obtain the total annual number of cases.
Results: The majority of patients had Pap III (n = 87; 88% vs. n = 12; 12% with Pap IV). The average age of patients was 39 years (22–75 years). The mean duration of treatment was 5.7 months (5.5 vs. 7.3 for Pap III and IV respectively), during which time patients had a mean of 4.19 consultations with gynecologists (4.1 vs. 5.1 for Pap III and IV respectively). The most common diagnostic tests used were Pap-smears (99%) and colposcopy (59%). Typically patients were treated by conisation (21% of Pap III vs. 67% of Pap IV) or hysterectomy (2% of Pap III vs. 25% of Pap IV). The average length of hospital stay for the treatment of Pap III was 0.9 days versus 7.6 days for Pap IV.
The total annual number of cases of Pap III was estimated at 238,381 and 34,587 for Pap IV.
Conclusion: The principal differences in the management and resource use of Pap III and IV were due to the significantly higher numbers of patients with Pap IV receiving surgical treatment, and having longer hospitalisations. The pre-cancer stages Pap III and IV are caused by HPV types 6, 11, 16 &18, and 16 & 18 respectively. There is evidence that using a vaccine targeting the most prevalent oncogenic HPV types (i.e. 16 and 18) could avert two-thirds of cervical cancer cases, and potentially decrease the economic burden of the disease. The impact of an HPV vaccine on the socio-economic burden of pre-cancerous cervical lesions needs further investigation.