addition, just before every field / every other field delivery, GS coordinates are obtain to estimate the organ motion and target volume repositioning if needed. Daily system implementation was evaluated for 15 patients undergoing IMRT to 72-80 Gy, depending on cases. Early toxicities grades and QOL questionnaire's data were analized.

Results: Sufficient quality DFFP system images of the gold seed were obtained on real time by the X,Y,Z coordinates of the center of a square delineating the seed; the center of the seed. An overall average of 4 system views per treatment fraction, taken from gantry 0 degrees, showed that intrafraction marker displacements were in the range of ± 1mm in 66.8% of delivered fractions. Compared to conventional techniques, in just a small number of all fractions (1/3), DFFP system-guided intrafraction "off range" marker positional corrections could be done, therefore reducing major motion uncertainties. High dose IMRT was well tolerated acutely, without grade 2 complications. Minimal urinary dysfunction and

867 POSTER

Thymidine phosphorylase (TP) expression in tumor cells of metastatic renal cell carcinoma (RCC) patients treated with capecitabine and interferon-alfa2A (IFNa).

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Background: TP is the rate-limiting enzyme that metabolizes 5'-deoxy-5-fluorouridine, an intermediate metabolite of capecitabine, to the active drug 5-fluorouracil (5-FU). Capecitabine is a fluoropyrimidine carbamate capable of exploiting the high concentrations of TP in tumor tissue to achieve activation preferentially at the tumor site, thereby minimising systemic exposure to 5-FU. Purpose of the study was to evaluate level of TP expression in tumor cells and correlation between TP expression and treatment efficacy of capecitabine and IFNa combination as the first line treatment in patients with metastatic RCC.

Material and methods: TP expression was evaluated in tumor tissue of 16 patients with immunohistochemistry assays using monoclonal anti-TP antibody (Roche Diagnostics GmbH). Semi-quantitative analysis by using a scoring system for tumor cells was performed, where staining percentage 0, 1-10%, 11-25%, 26-50%, >50% referred to as 0, 1+, 2+, 3+ and 4+, and staining intensity no staining, low, moderate and high intensity referred to as 0, 1+, 2+ and 3+. Semi-quantitative scores were calculated as sum of staining percentage and staining intensity scores, ranging from 0 to 7. Capecitabine was administered orally at a dose 1,250 mg/m2 twice daily for 14 days followed by 7 days of rest, IFNa was administered subcutaneously 6 million U three times weekly. Tumor measurements were performed after every 6 weeks.

Results: Overall response rate in this group of patients was 31%, all were partial responses, stable disease status was additionally achieved in 33% of patients. High level of TP expression (score e 5+) in tumor was detected in 9 patients from 16 (56%). All semi-quantitative scores and their relation to treatment effects are characterized in table:

		Best response (No. of patients)		
Score	No. of patients	Partial response	Stable disease	Progressive disease
2+	2	1	-	1
3+	2	1	-	1
4+	3	-	1	2
5+	3	-	2	1
6+	6	3	1	2
Total	16	5	4	7

Conclusions: Substantial TP expression in tumor tissue was detected in majority of patients with metastatic RCC. No correlation between TP expression and response to treatment with capecitabine and IFNa is possible to detect in analysed group of patients.

868 POSTER

A tolerance and efficacy study of thalidomide, paclitaxel, estramustine combination for patients with chemotherapy refractory androgen independent prostate carcinoma

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Background: Chemotherapy is effective palliative treatment (Rx) for patients (pts) with androgen-independent prostate carcinoma (AIPCa). Improvement in Rx is required. Results of salvage Rx in pts with AIPCA progressing after prior chemotherapy are under-reported. Preclinical studies indicate synergistic activity with combinations of anti-angiogenesis and cytotoxic agents. Thalidomide (T), an angiogenesis inhibitor, has single agent activity in AIPCa.

Material/Methods: We studied the combination of Paclitaxel (100 mg/m2/week, 2 out of 3 weeks), Estramustine (140 mg po q 8 hrs, 5 days/week, 2 out of 3 weeks) and escalating doses of T (200-400-600 mg/day) in pts with AIPCa, progressing after 1-2 prior cytotoxic regimens. Warfarin 2 mg po qd was given for deep venous thrombosis (DVT) prophylaxis. We considered that a $\geq$ 30% of pts with > 50% post-therapy PSA decline would be a clinically significant threshold of anti-tumor activity of the combination in this setting.

Results: To date, 26 pts [median age 66 (range, 49-80); median Zubrod performance status 1 (range, 0-2)] were entered (10 in the phase I and 16 in the phase II study) and received a median number of 3 (range, 1-8) cycles (C). Pts had 1 (n=18) or 2 (n=8) prior chemotherapy regimens (11 pts with prior Taxane/Estramustine-based Rx; 11 pts with prior Ketoconazole/Adriamycin/Vinblastine/Estramustine). Twenty-five pts are evaluable for toxicity (1 pt developed DVT prior to Rx initiation and did not receive any therapy); 19 are evaluable for response [2 pts were taken off study before 2 C (1 refused Rx after 1 week, 1 developed pneumonia after C1) and 4 pts are too early]. During C1 of the phase I study: at 200 mg/d T, 0 of 3 pts showed grade 3/4 toxicity; at 400 mg/d T, 1 of 4 pts experienced grade 3 neutropenia (< 7 days duration) and 1 of 4 pts had grade 3 edema (relieved promptly by diuretics); at 600 mg/d T, 0 of 3 pts had grade 3/4 toxicity. Of the 18 total pts assigned to the 600 mg/d dose level of T (in both phases of the study), 7 pts tolerated the 600 mg/d continuously, 8 pts tolerated 400 mg/d, 1 pt 200 mg/d, and 2 pts are too early. All dose reductions of T were due to somnolence/fatigue (grade 1-2). Peripheral neuropathy was limited to grade 1. Four of 25 pts developed grade 3/4 DVT (requiring Rx discontinuation in 2 pts), 2 additional pts discontinued Rx due to intercurrent infection, and 1 pt died from sepsis. To date, 15 of 19 (78%, 95% confidence interval 54-94%) evaluable for response pts achieved a sustained (more than 6 weeks duration) > 50% post-therapy decline in PSA, and 3 of 19 pts showed sustained > 80% post-therapy PSA decline. Measurable disease response and improvement in bone pain were seen.

Conclusion: These preliminary results show that a significant number of pts with AIPCa progressing after prior chemotherapy met the threshold of PSA decline considered of clinical significance, thus justifying further study of this combination in AIPCa.

869 POSTER

Gemcitabine (GEM) and oxaliplatin (l-OHP) to treat immunotherapy-resistant advanced renal cell carcinoma (ARCC) patients (pts.): preliminary results of a single institution phase II study

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Background: Pts. with aRCC still have a poor prognosis, with a median survival of approximately 10 months. Due to frequent overexpression of the MDR gene product, P-gp, RCC is a typical chemoresistant tumor, immunotherapy being consequently often used as first-line treatment option; furthermore, at present, there is no standard treatment for immunotherapy-unresponsive pts. Recently, however, combinations of newer chemotherapeutic agents, including GEM and, at a lesser extent, also L-OHP, have been shown to exert some antitumor activity in aRCC. Here we report the preliminary results of an ongoing single-institution phase II study.

Patients and methods: Twenty-five patients with aRCC unresponsive to s.c. IL-2 and IFN-α-based immunotherapy were treated to date with a combination of GEM (1,000 mg/m^2, i.v., days 1 and 8, q21) and L-OHP (90 mg/m^2, i.v., day 1, every 21); treatment was administered for a minimum of 2 cycles before response evaluation; toxicity was recorded at every cycle according to NCI-CTC.

Results: No complete response (CR) were observed, 3 pts. (12%, 95% CI: 2,5-31,2%) achieved a partial response (PR), 8 pts. (32%) had, as their best response, a disease stabilization (SD), while the remaining 16 pts. (56%) progressed (P). All three PR were observed after the first disease re-evaluation, i.e., after 2 cycles. As far as toxicity, treatment was generally well tolerated; indeed, no grade IV toxicity was observed, while grade III toxicity included myelosuppression (in 11 pts., i.e., 44%), neuropathy (in 10 pts., i.e., 40%) and non-neutropenic fever (in 7 pts., i.e., 28%); other, less severe, side effects included, nausea/vomiting, mucositis and fatigue.

Conclusions: Despite preliminary, our results suggest that the combination of GEM and L-OHP cannot improve the objective response rate

achieved with the combination of GEM and 5-fluorouracil in aRCC pts.; furthermore, our results showed an activity superimposible to that observed with the combination of GEM and Cisplatin. However, the high percentage of patients experiencing long-lasting SD, together with the good toxicity profile we observed, suggests that this regimen deserves further refining and evaluation.

870 POSTER

Long term follow-up in seminoma patients stage I and II A/B after adjuvant irradiation of lymphatic pathways

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Background: Adjuvant irradiation of the lymphatic pathways in seminoma patients is an established treatment. A long-term follow up of more than ten years is rarely reported in literature. The experience of a single institution is presented; recurrences and late effects were evaluated.

Materials and methods: From April 1981 to December 2000 179 patients with a seminoma received irradiation. From 174 patients the records could be evaluated. Median age was 37,8 years (21-74 years) Stage I 156 patients, II A 12 patients and II B 6 patients. In 86 patients the tumour was localized in the right testis, in the left in 84 patients. Histology showed in 167 patients a classical seminoma, in four a spermatocytic seminoma and in the remaining three an anaplastic seminoma. All patients underwent an inguinal orchiectomy followed by irradiation no chemotherapy was administered. Stage I patients received a median dose of 27,7 Gy (1982-1993 26-30 Gy, from 1993 26 Gy n=85), stage II A patients received a median dose of 31,7 Gy and in II B a median dose of 33,5 Gy. Irradiation was delivered with opposing fields using linear accelerator (n=172) and ^{60}Cobalt machine (n=2).

Results: Median follow up for all patients was 89 months. Recurrences occurred in five stage I patients and three stage II patients. One patient developed an isolated in-field recurrence after a dose of 30 Gy. The other locations were mediastinal n=4, inguinal n= 2 and supraclavicular n=1. All patients with recurrences received chemotherapy after biopsy (n=3) or partial surgery (n=3) leading to a complete second remission (median follow up: 66 months, range 5 to 121 months). Recurrence free survival at 10 years was for stage I 95,7% and for stage II 80,8%. Five patients died intercurrent. Overall survival was 91,3% and disease specific survival 100%. No late effects were observed.

Conclusion: The adjuvant irradiation of seminoma patients is well tolerated and able to minimize the risk of a lymph node recurrence. With regard to the benefit the side effects are acceptable.

871 POSTER

Acute toxicity and late GI and GU complications in organ sparing treatment of bladder cancer

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Purpose: To assess the factors predict acute toxicity and late GI and GU morbidity in radiation treatment of the bladder cancer. To investigate whether rectal and bladder volume which are in the treatment field can be used to identify risk groups for developing late gastrointestinal (GI) and genitourinary (GU) complications after organ sparing treatment of Bladder Cancer.

Method and Materials: A total of 41 patients with bladder cancer treated with definitive radiotherapy and with / without concomitant chemotherapy with a minimum of 3 years follow-up were evaluated. Patients were scanned with computerized tomography for treatment planning and treated with conventional box techniques. These patients were treated to a median total RT dose of 66.6 Gy at 1.8 Gy per fraction and 22 patients were treated with cisplatin 30 mg/m2 for 2h IV at weekly intervals in combination with RT. The irradiated rectal surface area for a given dose were calculated for a group of 41 patients treated with a four-field box techniques to a total (tumor minimum) dose range 64.8 to 68.4 Gy. The incidence of acute toxicity and late GI and GU complications was classified using the RTOG/ EORTC and the SOMA/LENT scoring system.

Results: Acute GI (7 patients) and GU (8patients) were noted grade 2 or higher side effects. Two patients had both side effects. GI acute side effects were not correlated with GU acute side effects. Late morbidities were not correlated with acute morbities. Two patients had grade 2 or 3 late effects of GI morbidities. Four patients had grade 2 or 3 late effects of GU morbidities. Higher T stage, involvement of pelvic lymph node and age(> 60 years) were significantly related to late GI and GU morbidity (p=0.061;p=0.014;p=0.001 respectively). The relative rectum wall and filling volumes which are in the treatment field correlated with acute toxicity and late GI complications. Relative bladder filling volumes also correlated with acute toxicity and urinary incontinence.

Conclusions: Both acute toxicity and late GI and GU morbidity demonstrated a volume dependence of rectum and bladder in the treatment field. Moreover both late GI and GU morbidity increased in patients more than 60 years old.

872 POSTER

Rectal toxicity and quality of life after definitive conformal radiation therapy (CRT) of patients with prostate cancer

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Background: To evaluate the impact of chronic rectal toxicity, especially rectal bleeding, on health related quality of life after definitive CRT of localized prostate cancer.

Material and methods: 173 patients were contacted a median of 46 months (24 98 m.) after CRT. Median age was 75 years (57 96 y.). Median dose to the prostate was 70 Gy (59 74 Gy). 80% of the patients had received short term neoadjuvant hormonal therapy before and during RT. Rectal toxicity was evaluated with a standardized 8-item toxicity score and rectal continence was evaluated with the Jorge and Wexner rectal continence score (JW-score). The EORTC quality of life questionnaire C30 (QLQ-C30, version 3) and the prostate cancer module QLQ-PR25 were used to evaluate quality of life. Analysis of variance was carried out to detect associations between rectal toxicity and quality of life.

Results: 25% of the patients stated to suffer presently from rectal bleeding: 10% experienced bleeding less than once/month, 10% had bleeding less than once/week and 5% reported at least weekly bleeding. The prevalence of the other rectal/bowel symptoms was: loss of mucous 10%, defecation pain 8%, bowel cramps 8%, flatulence 42%, diarrhea 26%, urge 27%. Overall 56% of the patients stated some kind of rectal incontinence on the JW-score (JW-score > 0). Rectal bleeding was not associated with global quality of life (QoL) nor with any other of the scales of the QLQ- C30. Patients with rectal bleeding had higher rectal symptom scores on the PR25 bowel scale ($p<0.001$) but rectal bleeding is one of it's items. None of the other rectal symptoms except for incontinence was associated with global quality of life. Patients with a rectal incontinence score of > 2 (n = 51) had worse QoL-values than those with a better or perfect continence (p=0.003). Age or the use of neoadjuvant hormonal therapy did not correlate with global quality of life.

Conclusions: Chronic rectal bleeding after CRT is common but it is mostly intermittent and it does not interfere with the patient's quality of life. Various degrees of rectal incontinence after CRT are frequent. Nevertheless only those patients with a JW-score of > 2 also report lower quality of life scores. Further research is needed to explore if there is an association between rectal continence and dose-volume histogram data.

873 POSTER

Predictors of late rectal and urologic side-effects after conformal radiation therapy (CRT) of patients with prostate cancer

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Background: To evaluate predictors of chronic rectal (GI) and urologic (URO) toxicity after CRT of prostate cancer.

Material and methods: 302 patients with a median follow up of 33 months (12 85 months) were evaluated. Median dose to the prostate was 70 Gy (59 74 Gy). 235 patients (78%) had received short term neoadjuvant hormonal therapy (HT) before and during RT. Toxicity was evaluated with a modified RTOG-score. Every macroscopic rectal bleeding was classified at least as grade II.

Results: Incidence of GI toxicity: table 1; Incidence of URO toxicity: table 2. No grade IV or grade V side-effects were observed.

Correlation of the following variables with grade II/III late toxicity was evaluated: Age, body mass index, prostate dose, inclusion of the seminal