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