tumor volume with cut-off values 150 and 1000 cm^3 ($p < 0.00001$), growth rate (cut-off 80 cm^3/mos.), ($p < 0.00001$), index of proliferation of tumor cells (cut-off 17%), (p=.03) and alkaline phosphatase (ALP) level ($p < 0.00001$). The multivariate model for stage IIB osteosarcoma included tumor volume (p=.07), ALP (p=.004) and growth rate (p=.01). Most favorable course of disease corresponding to stan-dard risk was observed in tumors smaller than 150 cm^3, low growth rate and normal ALP (tab.1). Predicted 5 yrs DFS in this cohort was 67%. In patients with tumor greater than 150 cm^3, growth rate >80 cm^3/mos. and elevated ALP level predicted 5 yrs DFS was under 20%. This combination corresponded to very high risk of disease progression.

Table 1. Risk assessment in osteosarcoma at presentation

Risk (predicted 5-yrs DFS)	Stage	Volume (cm^3)	Growth rate (cm^3/mo)	ALP
Standard (>60%)	IIB	<150	<80	normal
High (40−60%)	IIB	>150	<80	normal
		<1000	>80	normal
		<150	<80	elevated
Very high (<40%)				
	IIB	>1000	>80	normal
		>150	<80	elevated
		any	>80	elevated
	IIIB	any	any	any

Conclusions: The course of disease in osteosarcoma can be predicted at presentation. In order to avoid the overtreatment and chemotherapy associated morbidity, patients being at standard risk could be treated with standard intensity protocols. Three or four-drug up-front chemotherapy can be reserved for patients with high or very high risk. The advantages of risk adapted programs versus empirical approaches should be tested in prospective trials.

7516 POSTER

Cone beam CT for the estimation of setup errors in extremity sarcoma patients

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Introduction: Conventional setup verification during fractionated radiotherapy is performed by electronic portal imaging (EPI). Cone beam CT (CBCT) studies in other regions have demonstrated that EPI underestimates setup errors. This study compares the setup errors estimated by CBCT with errors estimated with EPI in extremity sarcoma patients.
Patients and Methods: 32 patients with primary extremity sarcomas (median age 51 years, range 25−70 years, 19 males and 13 females) were irradiated to a dose of 50−60 Gy in 25−30 fractions of 2 Gy. CBCT setup verification was performed in 13 patients and EPI in 19 cases, with the same offline correction protocol. Standard CTV-to-PTV margin is 10 mm in our current guideline.
Results: The estimated systematic error (1SD) of the initial patient setup (excluding corrections) is 1−2 mm larger in the CBCT group compared to EPI for all 3 directions: 4.6 mm versus 3.4 mm (left-right), 3.8 mm versus 2.4 mm (craniocaudal) and 3.6 mm versus 2.2 mm (dorsal-ventral), but these differences do not reach statistical significance. Using an off-line shrinking action level protocol, setup corrections were performed in 62% of the patients in de CBCT group and in 42% of the cases in the EPI group ($p = 0.28$). The mean number of corrections in the EPI population was 0.6 versus 1.3 in the CBCT group ($p = 0.07$).
Conclusion: EPI setup verification results in an underestimation of setup errors as compared with CBCT, but the differences are smaller than the CTV-to-PTV margins of 10 mm in current clinical protocols. However if intensity modulated radiotherapy techniques are considered with smaller margins, than CTV-to-PTV expansion should be larger if EPID is used for setup verification in comparison to CBCT.

7517 POSTER

Clinical tolerability of trabectedin administered by two different schedules (weekly for 3 of 4 weeks vs q3 weeks) in patients with advanced/metastatic liposarcoma or leiomyosarcoma (L-sarcomas) progressing despite prior treatment with at least anthracycline and ifosfamide

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Background: This international randomised study evaluated two trabectedin (T) iv schedules: 0.58 mg/m^2 3h weekly $\times$3/4 wk cycle (qwk 3h), and 1.5 mg/m^2 24h q3wk (q3wk 24h) in patients (pts) with advanced/metastatic L-sarcoma after failure of prior therapy with at least anthracycline and ifosfamide (60% also other agents – 33% gem/tax).
Methods: Safety/tolerability of T was analysed including adverse events (AEs), laboratory data and physical findings. MedDRA and NCI-CTC (version 2.0) were used to code AEs.
Results: 1473 cycles (cy) were administered (523 cy, qwk 3h; 950 cy, q3wk 24h) in 260 treated pts (130 pts on each regime). Median cy (range) was 2 (1−21) and 5 (1−37), respectively. Most T-related AEs were grade (gr) 1 or 2; 20% and 4% pts had gr 3 and 4 related AEs. Only 4 pts (3%; qwk 3h) and 8 pts (6%; q3wk 24h) discontinued T due to related AEs. Most common gr 3/4 related AEs were fatigue, nausea and vomiting, each affecting $\leqslant$5% pts and 1−2% cy. Gr 3/4 haematological toxicity was: neutropenia (qwk 3h: 13% pts, 6% cy; q3wk 24h: 47% pts, 21% cy), thrombocytopenia (qwk 3h: 6% pts, 1% cy; q3wk 24h: 12% pts, 2% cy) and anaemia (qwk 3h: 9% pts, 3% cy; q3wk 24h: 8% pts, 1% cy). Gr 3/4 neutropenia and thrombocytopenia were transient and of short duration (5−7 days). Febrile neutropenia was <1% pts in each group. Most common gr 3/4 biochemical toxicities were transient increases in AST/ALT (median duration 7−8 days). Liver toxicity was non-cumulative and no signs/symptoms of hepatic failure were observed. Deaths judged possibly related to T occurred in 2% (n = 3; qwk 3h) and 3% (n = 4, q3wk 24h) of pts.
Conclusions: The overall safety/tolerability of T was similar in both regimes, except for a higher incidence of haematological toxicity and transaminase changes in the q3wk 24h schedule, albeit without relevant clinical consequences. The expected rates of transient haematological toxicities and transaminase changes are consistent with those in prior T studies; these AEs were generally tolerable and manageable. Toxic death rates and discontinuations were low in the context of this pt population with advanced, heavily pretreated and poor prognosis disease. Of particular interest is the lack of many unpleasant effects frequently associated with cytotoxic agents such as alopecia, mucositis, skin/nail toxicities, neurotoxicity, or cardiac toxicity. T represents a reasonably well tolerated option for pts with L-sarcomas after failure of prior standard therapies.

7518 POSTER

The results of preoperative chemotherapy with or without radiotherapy in nonmetastatic high-grade osteosarcoma of the extremities

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Bacground: To assess the role of neadjuvant chemotherapy and adding of radiotherapy to the chemotherapy in patients with nonmetastatic high-grade osteosarcoma of the extremities and to compare the response of therapies on local control, tumor necrosis rate and overall survival rate.
Methods and Materials: Between 1987 and 2006, 75 extremity-localized nonmetastatic high grade osteosarcoma patients were treated with radiotherapy in our hospital. Forty-six patients were male and 29 patients were female. Median age was 17 years (11−66 years). All patients were treated with neoadjuvant chemotherapy. Chemotherapy schedule that was consisted of epirubicin, cisplatin and ifosfamide $\pm$ high dose methotraxate was given before surgery. In order to increase the chance of limb sparing surgery, preoperative radiotherapy was added to patients who refused amputation or whose limb-sparing surgery would