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

have been difficult because of borderline respectability. Radiotherapy was applied usually between the second and the third cycle of chemotherapy. Radiotherapy was given 35 Gy in 10 fractions to 47 patients. Remaining 2 patients were treated with 46 Gy with 2 Gy/day. Chemotherapy was given 3−6 cycles after surgery. In the radiotherapy group tumor size was between 3−32 cm (median 11 cm). In the chemotherapy group tumor size was between 4−20 cm (median 10 cm).
**Results:** Forty-seven patients out of 49 patients, who were treated with radiotherapy, had limb-sparing surgery. 24 patients out of 26 patients who were treated with only chemotherapy had limb-sparing surgery. On univariate analysis age $\leqslant$21 years ($p = 0.02$), lower extremity localization ($p = 0.003$) and HUVOS Grade IV ($p = 0.01$) significantly survived better than the others. On multivariate analysis HUVOS Grade ($p = 0.01$), age ($p = 0.02$) and tumor localization ($p = 0.003$) were significant prognostic factors for actuarial survival. In the radiotherapy group the 5-year local control, disease-free and actuarial survival rates were 98, 42 and 52, respectively. In chemotherapy group the 5-year local control, disease-free and actuarial survival rates were 91, 62 and 55, respectively.
**Conclusion:** Preoperative radiotherapy helps to increase the tumor necrosis rate, local control and the chance of extremity sparing surgery when combined with chemotherapy. Though overall survival rate was higher in patients with treated with chemotherapy, this difference was not statistically significant. It is difficult to make definite conclusions, because this was a nonrandomized and retrospectively analyzed study and the quality and the quantity of the patients were not the same in two groups.

**7519** POSTER

**Changing the treatment planning paradigm for soft tissue sarcoma in the thigh**

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**Purpose:** Post-operative radiotherapy in the thigh traditionally employs parallel-opposed fields covering the entire affected compartment, with large margins and minimal sparing of normal tissue. With the change in surgical techniques and the move from 2D to 3D radiotherapy planning, this study explored conventional radiotherapy treatment volumes and compared them to conformal treatment of the tumour bed with margins adapted according to normal tissue dose constraints. Conventional volumes were compared to tumour bed volumes for length and volume and IMRT dose/volume constraints were constructed.
**Materials and Methods:** Radiotherapy planning CT scans of 10 patients with soft tissue sarcoma of the thigh were acquired. Volumes were defined using pre-operative imaging, surgical notes, pathology and surgical clips placed in the tumour bed. Conventional volumes were defined as the whole of the involved compartment of the thigh, with a radial margin of 1 cm to form the Phase I PTV. Superior/inferior (S/I) margins of 5 cm were added for tumours less than 10 cm length and 7 cm for tumours over 10 cm length. Conformal plans were defined as the tumour bed, a 3 cm radial margin was added and 5 cm S/I. Organs at risk (OAR) were identified as whole femur, neurovascular bundle, a soft tissue corridor and normal tissue outside the PTV. Pelvic organs were contoured for four patients whose disease involved the insertion of the muscle group.
**Results:** The planning protocol defined modifications of the conformal PTV for OAR extension. A skin corridor was defined as a 2 cm margin opposite to the PTV, covering 1/3 of the thigh circumference over the length of the PTV. The median volume (range) of the conformal CTV was 335 cc (57–1088 cc) compared to 712 cc (222–1544 cc) for the conventional plans ($p = 0.009$). The median volume (range) of the conformal PTV was 1813 cc (597–3919 cc) compared to 2743 cc (1130–5133 cc) for the conventional PTV ($p = 0.02$). The median length of PTV was 26 cm for the conformal plan and 29 cm for the conventional plan ($p = 0.04$).
**Conclusion:** Defining the CTV according to the surgical tumour bed rather than the affected compartment results in a significantly lower PTV volume and treatment field length enabling the definition of a prospective IMRT outlining protocol. Use of reduced treatment volumes and IMRT techniques may result in lower doses of radiation to critical normal tissues and therefore to decreased late side effects and may allow for conformal dose escalation.

**7520** POSTER

**Preoperative IMRT combined with temozolomide for locally advanced soft tissue sarcoma**

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**Background:** Neoadjvuant radiation has shown to improve local tumor control in soft tissue sarcoma. This study was conducted to evaluate the toxicity and therapeutic effects of preoperative intensity-modulated radiation therapy (IMRT) combined with temozolomide.
**Patients and Methods:** Eligibility included primary high-grade soft tissue sarcoma or recurrent tumors not amenable to surgical resection with clear margins. Patients received 50 mg/m$^2$ Temozolomide during IMRT (50.4 Gy, 28 $\times$ x 1.8 Gy). Resection was intended six to eight weeks after completion of neoadjuvant treatment. Toxicity was assessed by NCI-CTC 3.0 and response was assessed by MRI using RECIST criteria as well as by pathology of the resection specimen using the proportion of necrosis for classification.
**Results:** Thirteen patients were enrolled and twelve patients completed the protocol. One patient stopped treatment because of tumor related abdominal pain. No grade four toxicities have been reported. Most frequent grade three toxicity was nausea and vomiting (6/13). Most frequent toxicities of any grade have been dermatological (9/13), gastrointestinal (8/13) and haematological (7/13). Local response according to RECIST criteria was progressive disease in three patients, stable disease in six and partial response in four cases. Two patients developed intercurrent lung metastases. Eight patients underwent surgery, of which five were R0 and three were R1 resections. Four patients did not undergo surgery because of metastatic disease or unresectability and one patient refused surgery. Wound complications occurred in two patients. Histologic examination revealed more than 90% necrosis in one resection specimen, more than 50% in four cases and less than 50% in another three.
**Conclusion:** Preoperative chemoradiation with temozolomide and IMRT for locally advanced soft tissue sarcoma can be administered safely and with some efficacy in patients with locally advanced soft tissue sarcoma. The histological response to treatment leaves room for further exploratory trials.

**7521** POSTER

**Successful pan-European and trans-Atlantic collaboration in a randomised controlled trial in osteosarcoma: EURAMOS1 (ISRCTN67613327; a trial conducted as part of ECT-EUROCORES)**

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**Background:** Randomised controlled trials (RCT) are the gold standard for assessing new approaches to treatment. In rare cancers, such as osteosarcoma, RCTs can only be performed with large-scale international cooperation and collaboration.
**Materials and Methods:** Four multinational groups (COG, COSS, EOI, SSG) from Europe and North America collaborate in EURAMOS1 within the European Science Foundation's ECT-EUROCORES scheme, led from MRC Clinical Trials Unit (London, UK). All patients receive MAP chemotherapy (methotrexate, doxorubicin and cisplatin) prior to surgery and are risk-stratified after surgery: "good responders" are randomized to continued MAP or MAP followed by maintenance pegylated interferon; "poor responders" are randomized to either continued MAP or MAPIE (MAP + ifosfamide, etoposide). 1400 registered patients are planned over 4 years. An efficient infrastructure has been set up to ensure the successful running of the trial. The EURAMOS Intergroup Safety Desk (Muenster, D) has established an international system for SAE, SAR & SUSAR reporting to multiple competent authorities and ethics committees. Trial site monitoring and data centre audits are well under way. ESF has funded two training courses to familiarize institutional staff with the requirements of multinational GCP trials; a third is planned.