frequent G3/4 non-haematological toxicities were asthenia (10%), nausea and vomiting (4% and 6%). Four deaths were considered treatment-related (those pts had contraindications to receive T and/or violation of dose guidelines). Efficacy (WHO criteria) in 75 STS pts was: 7 PRs and 24 SD (including 2 minor responses [MR]). Overall response rate (ORR): 10% (95% CI: 4−18); *m*PFS: 1.6 months (mo) (95% CI: 1.4−2.8), *m*OS: 10.5 mo (95% CI: 6.6−14.3) and *m* duration of response (*m*DR): 4.6 mo (95% CI: 2.1−7.1). Bone sarcoma pts (n = 25) had: 3 PR and 4 SD (including 2 MR); ORR: 12% (95% CI: 2−31) with *m*PFS: 2.1 mo (95% CI: 1.1−3.2), *m*OS: 7.1 mo (95% CI: 3.6−10.5) and *m*DR: 2.9 mo (95% CI: 2.1−3.6). The overall clinical benefit (PR+MR/SD>6mo) for all populations was 17%.
**Conclusions:** T given as a 3-h infusion q3wk is safe and can be given on an outpatient basis to heavily pre-treated pts with advanced sarcoma. The observed clinical benefit is noteworthy, given the degree of pre-treatment and tumour burden in this population.

**9427** POSTER

**Efficacy of second-line trabectedin in patients with advanced liposarcomas and leiomyosarcomas progressing despite prior conventional chemotherapy**

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**Background:** The efficacy of trabectedin every 3 weeks, 24-h infusion (q3wk-24h) was compared vs. a weekly regimen over 3-h (qwk-3h) in an international randomized trial of 270 patients (pts) with liposarcomas and leiomyosarcomas progressing despite prior therapy with at least an anthracycline and ifosfamide. Outcomes of 1.5 mg/m$^2$ in the q3wk-24h arm were significantly better than those in the weekly regimen: median number of cycles 5 (1−37) vs. 2 (1−21); median time to progression (TTP) 3.7 vs. 2.3 mo. [HR: 0.734; p = 0.0302]; median progression free survival (PFS) 3.3 vs. 2.3 mo. [HR: 0.755; p = 0.0418]. Median survival (n = 175 events) 13.8 vs. 11.8 mo. [HR: 0.823; p = 0.1984] (ASCO 2007). European Commission approval was based mainly on these data. The objective of this pos hoc analysis is to present information from the subset of pts treated with trabectedin as a second-line regimen.
**Methods:** 93 pts received trabectedin as second line (n = 47 q3wk-24h and n = 46 qwk-3h). Median number of cycles, TTP, PFS, tumor control rate and overall survival (OS) were analyzed. Endpoints were assessed by independent review. All pts had progressed to one prior treatment with an anthracycline plus ifosfamide.
**Results:** In the q3wk-24h vs. qwk-3h arms median number of cycles were 6 (1−25) vs. 4 (1−14); median TTP 4.4 mo. 95% CI (2.0−7.6) vs. 3.6 mo. 95% CI (2.1−6.8) HR: 0.82 p = 0.4231; TTP at 6 mo. 41.9% 95% CI (27.3−56.5%) vs. 38.0% 95% CI (22.7−53.3%); median PFS 4.4 mo. 95% CI (2.0−7.6) vs. 3.6 mo. 95% CI (2.3−6.8) HR: 0.833 p = 0.4502; PFS at 6 mo. 41.0% 95% CI (26.6−55.4%) vs. 38.3% 95% CI (23.7−53.0%). Three (6.4%) partial responses (PR) and 23 (48.9%) stable disease (SD) (SD$\geqslant$6 mo. 27.7%) vs. 1 (2.2%) PR and 24 (52.2%) SD (SD$\geqslant$6 mo. 23.9%) were seen in the q3wk-24h vs. qwk-3h, respectively. OS at 36 mo. was 23.9% 95% CI (11.4−36.5%) vs. 16.2% 95% CI (5.3−27.0%). The safety profile of trabectedin in this subset was manageable and in line with prior experience.
**Conclusions:** Efficacy outcomes were better in the subset of pts receiving trabectedin after failure of first-line anthracycline + ifosfamide relative to pts with more extensive prior therapy, with similar safety profile. Consistent with the results in the overall population, longer TTP and PFS were found with trabectedin q3wk-24h.

**9428** POSTER

**Experience in high-dose chemotherapy with peripheral stem cell rescue and biotherapy for young adults with high-risk Ewing/PNET sarcoma**

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**Background:** The Protocol MMES-99 (Minsk-Moscow Ewing's Sarcoma) includes the induction chemotherapy (CT) and the consolidation (resection and/or radiation therapy (RT)) and the high-dose CT with peripheral stem cell rescue (PSCR) and biotherapy with interleukin-2 (Roncoleukin®). The objective of this study is evaluation of tolerance and efficacy of the MMES-99 Protocol in young adults.
**Materials and Methods:** Induction phase consists of 5 or 6 courses of CT, A–B–A–B–A (course A: cyclophosphamide 4.2 g/m$^2$ + doxorubicine 75 mg/m$^2$ + vincristine 3 mg/m$^2$ (1.5 mg/m$^2$, days 1 and 8); course B: ifosphamide 12 g/m$^2$ + etoposide 500 mg/m$^2$). The harvest of PSC was performed after the 2nd−3rd course. Local RT (a total target dose (TTD) of 51 Gy, a hyperfractionated schedule) or surgery was administered after the 5th course, followed by the high-dose CT. In case of prolonged intervals between the courses of local RT (more than 4 weeks), the patients received the course C (vincristine 3 mg/m$^2$ + cyclophosphamide 4.2 g/m$^2$). Patients with pulmonary metastases were administered RT on lungs after the 2nd course (TTD 12 Gy). High-dose CT: busulfan 16 mg/kg, thiophosphamide 600 mg/m$^2$, melphalan 140 mg/m$^2$. We present the results of treatment of 10 patients (the median age 21.5 years (range 17−26)). In two cases the treatment was started in progression disease. Lesions: 2 – spine, 1 – spine+lungs, 1 – skull, 2 – pelvic bones (505 ml and 393 ml), 1 – clavicle (450 ml)+lungs, 1 – humerus (1290 ml), 1 – femoral bone (160 ml), 1 – multicentre involvement of bones+lungs. EWS and EWS-ERG genes in blood and bone marrow were negative before harvest of PSC.
**Results:** 54 courses of induction CT were administered. Harvest of PSC and subsequent high-dose CT were performed in 8 patients (median value of CD34 $3.5 \cdot 10^6$/kg; median number of nucleated cells $4.0 \cdot 10^8$/kg). Two patients did not undergo harvest of PSC due to infectious complications and no response to induction therapy. Five patients received Roncoleukin®. A total of 66 immunotherapy courses were administered, the mean single dose of Roncoleukin® was 2.7 mg, the mean protocol dose 49.5 mg. The immediate clinical effect was 90%. The progression-free survival rate was $0.67 \pm 0.27$ (median follow-up before progression 20.0 months). Grade 4 induction toxicity (CTCAE): leukopenia 81.4%, thrombocytopenia 29.6%, anemia 7.4%, infectious complications 16.7%.
**Conclusion:** Intensive induction therapy followed by high-dose CT and interleukin-2 biotherapy for young adults (before 30 years) with Ewing's sarcoma is a treatment of choice with adequate supportive therapy.

**9429** POSTER

**Long-term toxicity in survivors of bone tumors diagnosed at adult age: a plea for systematic screening and timely intervention**

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**Background:** It is well known that survivors of childhood cancer may experience late toxicity of therapy. Survivors of bone tumors appear the most severely affected, which is explained by the specific combination of cytotoxic drugs and often major surgery. We know of no systematic screening for late events in survivors of malignant Ewing's sarcoma (ES) and osteosarcoma (OS) treated at adult age and therefore initiated the following study.
**Patients and Methods:** Patients who had been diagnosed with OS or ES at age 16 or over and treated at adult departments of the Radboud University Nijmegen Medical Center between 1982 and 2007 were identified. Those who are currently alive and relapse-free were invited for a systematic screening for late toxicity, consisting of history taking and physical examination, Multi Gated Acquisition (MUGA) scan, echocardiogram, dual energy x-ray absorptiometry (DEXA), audiogram,

serum and urine screening for renal toxicity, fertility (sex hormone levels, Inhibin B and anti-Müllerian hormone) and metabolic syndrome trait (lipid profile, fasting glucose).
**Results:** Currently 20 patients (70% male, median age 45 years [19−66], median follow-up 9.5 years [2−27], 65% OS) have been enrolled in the study. Eight patients (40%) reported ongoing fatigue, 5 (25%) were unwillingly unemployed and 2 (10%) reported involuntary childlessness. In 2 patients a subclinical cardiomyopathy was found with a left ventricle ejection fraction of 40% and 47%, respectively (N>55%). Only one patient with metabolic syndrome was identified. Low bone mineral density (osteopenia or osteoporosis) was found in 12 patients (60%), major hearing impairments in 4 (20%). Renal toxicity was also frequently found with a glomerular filtration rate $\geqslant$1 SD below the age- and genderspecific reference value in 6 patients (30%) and tubular nephropathy in 12 (60%).
**Conclusions:** The prevalence of long-term toxicity was high in the first 20 adult OS en ES survivors included in this study. The most striking findings were 2 cases of previously undetected cardiomyopathy, tubular nephropathy in more than half of the patients and – unexpectedly – low mineral bone density in 60% of the patients. These findings have clinical relevance since therapeutic options are available to prevent further deterioration. In our opinion, survivors of ES and OS diagnosed and treated at adult age should be screened for late events in a systematic manner analogous to common practice in children's oncology departments.

**9430** POSTER

**Efficacy and toxicity of sorafenib in patients with advanced soft tissue sarcoma failing anthracycline-based chemotherapy**

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**Background:** Sorafenib, an orally administered inhibitor of RAF-family serine/threonine kinases and tyrosine kinase receptors, has demonstrated promising results in the treatment of refractory advanced solid tumors, including soft tissue sarcoma (STS), in terms of disease control and toxicity profile. We performed a multicenter phase II study aimed to evaluate the efficacy and safety of sorafenib in patients with advanced STS progressing after anthracycline-based chemotherapy.
**Methods:** Patients with recurrent STS failing at least one line of chemotherapy and no relevant comorbidities were eligible for the study and received sorafenib 400 mg bid until progression or major toxicity. Patients who received the study drug for at least 4 weeks were considered evaluable for statistical analysis. Primary endpoint of the study was the rate of progression free survival (PFS) at 6 months; the overall clinical benefit, i.e. the proportion of patients achieving response (partial, PR, complete, CR) or stable disease (SD) lasting at least 3 months (RECIST criteria) was also evaluated. Toxicity was graded according to the NCI Common Toxicity Criteria V3.0.
**Results:** Among 74 patients enrolled in the study, at march 30, 2009, 40 and 44 patients were evaluable for response and toxicity, respectively. Most frequent pathologic subtypes were leiomyosarcoma and liposarcoma. About half of patients received sorafenib as third or subsequent line of treatment. Six-months PFS was observed in 10/40 (22.7%) while overall clinical benefit was documented in 24/40 patients (60%, CR = 0%, PR = 12.5, SD = 47.5). Most frequently reported adverse events were fatigue, anemia, weight loss, diarrhoea, hand-foot syndrome (HFS) and alopecia. Grade 3−4 toxicities included HFS in 15.9%, diarrhoea in 13.6%, anemia in 4.5% and mucositis in 4.5%.
**Conclusion:** Sorafenib is associated with antitumor activity and acceptable tolerability in patients with antracycline-refractory STS. Data from the whole patient population will be presented at the meeting.

**9431** POSTER

**The role of radiotherapy for aggressive fibromatosis**

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**Background:** Aggressive fibromatosis is a benign mesenchymal tissue proliferation. Surgery is the preferred treatment but the infiltrative growth pattern predisposes to local recurrences if wide margins are not obtained. Repeat surgery may be morbid and risk further recurrences. Alternative approaches can therefore be considered. Radiotherapy (RT) is an option and single institution series have shown benefit of radiotherapy in terms of local control. Radiotherapy may also be considered as an adjuvant treatment for patients with high risk of local failure after surgery, particularly in surgically challenging anatomical areas.
**Materials and Method:** A retrospective review of all patients with fibromatosis, treated with conformal RT, seen at The Christie Sarcoma Clinic from 2000 to 2009 was performed. Data on patient characteristics, tumour site, RT and clinical outcomes was extracted.
**Results:** Forty-five patients with fibromatosis were identified. Eleven patients (six females and five males) received RT. Age range was 19−70 years. Tumour sites were upper limb girdle (4), head and neck (2), chest wall (2), lower limb (1), flank (1) and intra-thoracic (1). Primary treatment was RT in four inoperable cases and surgery in seven. Of these seven, three received adjuvant RT for high risk disease and four received RT for subsequent disease progression. Doses ranged from 45−56 Gy in 25−28 fractions (mean dose 47 Gy). Two patients were treated in an EORTC phase II study. Median follow up was 30 months (range 1−99 months). The 3 patients who had adjuvant RT were disease free at last follow up (median follow up 51 months). Of the remaining 8 who had progressive disease at the time of RT, 5 had continued response to treatment or stable disease with no additional systemic treatment. Three had progressive disease (2 outside RT field) at 10, 21 and 48 months after radiotherapy. Two required further systemic treatment and one stabilised without intervention.
**Conclusion:** The small numbers in this study reflect the rarity of this disease, so it is best managed within the multi-disciplinary soft tissue sarcoma team. Conformal radiotherapy may be a viable option for inoperable symptomatic disease or in relapsed cases, particularly in anatomically constrained areas, which risk causing considerable morbidity and limited chances of obtaining wide margins. Adjuvant radiotherapy merits further research.