progressing despite prior therapy with at least anthracyclines (A) and ifosfamide (I). Primary endpoint was time to progression (TTP) assessed by independent review; response rate (RR), progression-free (PFS) and overall survival were secondary endpoints. In the protocol-specified primary analysis, TTP ($p = 0.030$; HR 0.73) and PFS ($p = 0.042$; HR 0.75) were significantly better with the q3wk 24h T schedule, in spite of a modest 5.6% (12% per investigators) RR by RECIST. Acknowledging the limitations of RR by RECIST as a surrogate for clinical benefit in sarcomas, 3 supportive analyses were conducted: Clinical Benefit Rate (CBR), Growth Modulation Index (GMI) and Maximum % of Tumour Variation (MTV).
Methods: CBR was defined as the sum of CR+PR+SD?24 wks. MTV was calculated as: (minimum sum of longest diameters [SLD] of all lesions before or at PD date – SLD at baseline)/(SLD at baseline)·100 (212 pts evaluable). GMI (intrapatient-specific historical control) was calculated as: TTP with T / TTP with prior chemo for advanced/metastatic sarcoma (218 pts evaluable; data prospectively collected). A GMI >1.33 (TTP with $T \geqslant 33\%$ prior TTP) was judged as indicative of pt benefit.
Results: CBR and MTV were significantly better with the q3wk 24h T schedule. CBRs of 39% and 24% were achieved with the q3wk 24h and qwk 3h schedules (Fisher's; $p = 0.022$). MTV showed tumour shrinkage in target lesions in 51% pts in the q3wk 24h arm vs 32% in the qwk 3h arm (Mann-Whitney-Wilcoxon; $p = 0.0008$). Most pts (67%) had bulky tumours at study entry. GMI > 1.33 was achieved in 37% (q3wk 24h) and 31% (qwk 3h) of pts. Last prior chemo was A+I in 48% of pts, gemcitabine-based regime (17%), single-agent I (13%) and others.
Conclusions: The outcomes with the less efficacious qwk 3h arm support this T schedule as an active control. However, consistently better outcomes were seen with the q3wk 24h T schedule. Overall, these results add biological plausibility to the significantly better outcomes in the primary endpoint TTP seen with T q3wk 24h and provide confidence in the clinical relevance of the overall findings. CBR, GMI and MTV, if adequately applied, appear more useful endpoints than conventional RR per RECIST to detect clinical benefit in pts with advanced/metastatic sarcomas.

7513 POSTER

Impact of local management on long-term outcomes in Ewing's tumor of the pelvis: the University of Florida experience

D.J. Indelicato[1], S.R. Keole[1], A.H. Shahlaee[2], C.G. Morris[3], C.P. Gibbs[4], M.T. Scarborough[4], R.B. Marcus[5]. *[1]University of Florida, Radiation Oncology, Gainesville Florida, USA; [2]University of Florida, Pediatric Oncology, Gainesville Florida, USA; [3]University of Florida, Statistics/Radiation Oncology, Gainesville Florida, USA; [4]University of Florida, Orthopedic Oncology, Gainesville Florida, USA; [5]Emory University, Radiation Oncology, Atlanta Georgia, USA*

Purpose: Comprehensive reports of long-term outcomes are limited but nonetheless crucial to the debate regarding local management of pelvic Ewing's tumor. This retrospective analysis describes our 35-year experience with respect to disease control and functional status.
Patients and Methods: Thirty-five patients with localized Ewing's tumors of the pelvis were treated from 1970–2005. Twenty-six patients were treated with definitive radiotherapy (RT) and 9 patients were treated with combined local therapy in the form of surgery + RT (8 preoperative and 1 postoperative). The median RT dose was 55.2 Gy. The patients who received RT alone were more likely to be older males with larger tumors exhibiting soft-tissue extension. All patients received standard chemotherapy. Patients in the definitive RT group were more likely to receive etoposide and ifosfamide or undergo bone marrow transplant. Median potential follow-up was 19.4 years. Functional outcome was assessed using the Toronto Extremity Salvage Score (TESS).
Results: 5-year absolute rates of local control and cause-specific survival in the post-1985 era have increased by 2% and 24% respectively. The 15-year actuarial overall survival, cause-specific survival, freedom from relapse rate, and local control rates were 26% vs. 76% ($p = 0.016$), 26% vs. 76% ($p = 0.016$), 28% vs. 78% ($p = 0.015$), and 64% vs. 100% ($p = 0.087$), respectively, for patients treated with definitive RT and combined therapy. Overall, tumors <8 cm had significantly better cause-specific survival but this was unrelated to local control. The median TESS for the definitive RT and combined therapy groups were 99 and 94 respectively ($p = 0.19$). Six definitive RT patients (23%) had serious complications including two secondary malignancies, a pathologic fracture, and osteoradionecrosis requiring hip replacement. Bowel perforation was the only serious complication observed in the combined therapy group.
Conclusion: Despite improvement in cause-specific survival over the past 35 years, we have made little progress in terms of local control. A small subset of eligible patients may benefit from complete excision, but rates of disease control and complication are poor when it is necessary to treat Ewing's tumors of the pelvis with RT alone. Most patients have unresectable tumors and therefore innovative RT strategies are needed to improve long-term disease outcomes and minimize side effects while maintaining an acceptable functional result.

7514 POSTER

Long-lasting St. Jude Hospital protocol in adult Ewing sarcoma patients

A.S. Ataergin[1], A. Ozet[1], F. Arpaci[1], M. Turan[2], C. Ulutin[3], M. Ozturk[1], F. Kilicli[1], B. Ozturk[1], S. Komurcu[1], O. Kuzhan[1]. *[1]GATA Faculty of Medicine, Medical Oncology and BMT Unit, Ankara, Turkey; [2]GATA Faculty of Medicine, Hydroclimatology, Ankara, Turkey; [3]GATA Faculty of Medicine, Radiation Oncology, Ankara, Turkey*

Background: Adult patients with Ewing sarcoma may achieve long-term survival with local treatment modalities and systemic chemotherapy. Although chemotherapy is effective in this setting, a standard chemotherapy regimen is not yet developed. In this study, the feasibility and the effectiveness of long-term ewing sarcoma protocol of St. Jude Hospital.
Materials and Methods: Twenty-five adult patients with ewing sarcoma (22 males, 3 females) received 41-week St. Jude Hospital protocol. The protocol consisted of induction chemotherapy applied within weeks 0 to 6 (ifosfamide 2 g/m2/day, days 1−3, etoposide 150 mg/m^2/day, days 1−3, cyclophosphamide 1.5 g/m2 day 5, doxorubicin 45 mg/m^2 day 5); on the 9th week surgical resection with or without radiotherapy was done, followed-by vincristin 1.5 mg/m^2, D-actinomycin 1.5 mg/m^2 within weeks 11 and 17 and the maintenance treatment within weeks 20 and 41 (ifosfamide 2 g/m2/day, days 1−5; etoposide 150 mg/m^2/day, days 1−5; cyclophosphamide 1/m2/day, days 1 and 2; doxorubicin 60 mg/m^2 day 1, as continuous infusion in 24 hours). All chemotherapy regimens were given every three weeks.
Results: The median age of the patients was 23 (range: 18−55). The initial stage of the disease was IIB in 20 cases, and IV in 5 cases. In 10 cases tumor was originated from the extremity, and in 14 cases from other bones from the extremities. Forteen cases underwent surgical resection and 22 cases were given radiotherapy for local control. All cases completed the treatment protocol. The median duration of chemotherapy was 44 weeks (range: 41−56). Twelve cases (48%) achieved complete response, 7 cases (28%) achieved partial response, whereas 5 cases (20%) had progression after the completion of the protocol. Thirteen cases (52%) developped myelotoxicity, 2 cases (0.08%) developped nefrotoxicity, 2 cases (0.08%) developed neurotoxicity, and 3 cases (12%) developed angina pectoris during the treatment protocol. No dose reduction or modification was made in the patients. In 11 patients (44%) G-CSF was used, 13 patients (52%) were given erytocyte transfusions. 4-year overall survival rates were 43% in stage II patients and 40% in stage IV patients, respectively. 4-year disease-free survival rates were 25% in stage II patients and 20% in stage IV patients, respectively.
Conclusions: In conclusion, the long-lasting St. Jude Hospital protocol was found similar to other chemotherapy protocols in regard to toxicity and survival in adult patients with Ewing sarcoma.

7515 POSTER

Prognostic factors in osteosarcoma. The arguments for risk adapted up-front treatment

G. Machak[1], B. Bokhian[1], N. Kochergina[1], O. Senko[2], M. Aliev[3]. *[1]N.N. Blokhin Russian Cancer Research Center, general oncology, Moscow, Russian Federation; [2]Computer Center of RAS, pattern recognition group, Moscow, Russian Federation; [3]N.N. Blokhin Russian Cancer Research Center, general oncology, Moscow, Russian Federation*

Background: The response to induction chemotherapy is the standard criteria for risk assessment in osteosarcoma. In order to evaluate the risk earlier, we have investigated several pretreatment tumor related characteristics.
Materials and Methods: The database included 593 patients treated at the N.N. Blokhin Russian Cancer Center. Between 1979 and 1986, preoperative treatment comprised one 72-hour IA infusion of DOX 90 mg/m^2 and radiotherapy 40 Gy. From 1986 to 1999 induction chemotherapy consisted of 3−5 monthly cycles of IA DOX 90 mg/m^2 or CDDP 120 mg/m^2. In both protocols 6 cycles of CAP (cisplatin 100 mg/m^2 + doxorubicin 60 mg/m^2 + cyclophosphamide 600 mg/m^2) chemotherapy were administered after removal of primary. The last protocol consisted of 3−4 cycles of intensified induction chemotherapy with DOX 90 mg/m^2 and CDDP 120 mg/m^2 IV or IA, surgery at week 20 and 6 cycles of adjuvant chemotherapy with DOX, CDDP, IFO (standard dose) and VP-16. Cox regression was used for multivariate analysis.
Results: The following pretreatment factors were predictive for disease-free survival (DFS) in univariate analysis: stage by Enneking ($p < 0.00001$),

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

R. Haas, A. Betgen, W. Oughlane-Heemsbergen, P. Remeijer. *The Netherlands Cancer Institute, Radiotherapy, Amsterdam, The Netherlands*

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

S. Chawla[1], P.G. Casali[2], M. von Mehren[3], A. Le Cesne[4], J.Y. Blay[5], C. Lebedinsky[6], V. Alfaro[6], Y. Elsayed[7], B. Michiels[7], G.D. Demetri[8], on behalf of Yondelis Sarcoma Study Group. *[1]Century City Hospital, Oncology, Los Angeles, USA; [2]Istituto Nazionale Tumori, Oncology, Milano, Italy; [3]Fox Chase Cancer Center, Oncology, Philadelphia, USA; [4]Institut Gustave Roussy, Oncology, Villejuif, France; [5]Center Leon Berard, Oncology, Lyon, France; [6]PharmaMar, Oncology, Madrid, Spain; [7]Johnson & Johnson, Oncology, Raritan, USA; [8]Ludwig Center at Dana-Farber/Harvard, Oncology, Boston, USA*

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

N.M. Mandel[1], F.O. Dincbas[2], D.C. Oksuz[2], S. Koca[2], S. Dervisoglu[3], B.C. Bicakci[2], H. Secmezacar[4], H. Turna[1], K. Kanberoglu[5], M. Hiz[4]. *[1]Cerrahpasa Medical Faculty, Medical Oncology, Istanbul, Turkey; [2]Cerrahpasa Medical Faculty, Radiation oncology, Istanbul, Turkey; [3]Cerrahpasa Medical Faculty, Pathology, Istanbul, Turkey; [4]Cerrahpasa Medical Faculty, Orthopedic Surgery, Istanbul, Turkey; [5]Cerrahpasa Medical Faculty, Radiology, Istanbul, Turkey*

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