Methods: From 2005 to 2008, nine patients (7 women and 2 men), mean age 52.3±12.6 years, with RPS were treated with pre-operative IMRT. Toxicities, loco-regional control, and survival free disease were analyzed. Toxicity was assessed according to the RTOG acute toxicity scale.
Results: Four patients (44%) had de novo RPS, and five patients (56%) had recurrent RPS after prior surgical resection. The median follow up was 26 (range: 3−39) months after radiotherapy. Median radiation dose was 50 at 2 Gy/fraction. Surgical resection after radiotherapy was performed in eight patients. In one patient, tumor progressed during treatment and was unresectable. Only minor toxicities were reported with grade 1 nausea in seven patients (77%) and vomiting in two patients (22%), during radiotherapy. No other toxicities or treatment related deaths were reported. Early and delayed postoperative complications included 1 abscess and 1 duodenal stenosis in two patients. At median follow up of 26 months, four patients (44%) were disease free. Five patients (56%) had disease progression, including tumor progression during radiotherapy (2 pts, 22%), local recurrence after surgery (2 pts, 22%), and/or distant metastasis resulting in death (2 pts, 22%). Four (80%) of the five patients with recurrent RPS after prior surgical resection, had disease progression.
Conclusion: Local control of de novo RPS is achievable with pre-operative IMRT with minimal toxicities. Henceforward, low toxicities with IMRT could allow dose escalation to improve outcomes in RPS patients.

9424 POSTER

Radiotherapy results of 131 patients with soft tissue sarcoma

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Background: In this retrospective study, our records of the patients with soft tissue sarcoma who underwent postoperative or definitive radiotherapy at Hacettepe University Faculty of Medicine Department of Radiation Oncology between January 1994 and December 2006 were reviewed. Cases were divided into two groups according to their location whether in the retroperitoneal region or not.
Material and Methods: Patients with soft tissue sarcoma excluding retroperitoneum, total of 101, median age 47; and patients with retroperitoneal sarcoma, total of 30, median age 53, were evaluated. In excluding retroperitoneum group, 37 of our patients were stage I, 24 were stage II, 37 were stage III, and 3 were stage IV (no distant metastasis, lymph node positive). According to histological degree, 5% cases were 1st, 36% cases were 2nd and 59% cases were 3rd or 4th degree. In retroperitoneal sarcoma group, 17 of our patients were stage I, 1 were stage II, 12 were stage III. According to histological degree, 7% cases were 1st, 50% cases were 2nd and 43% cases were 3rd or 4th degree. In all patients with 1.8−2.5 Gy per fraction total of 40−70 Gy radiotherapy doses were delivered (the median 60 Gy in excluding retroperitoneum group while 50 Gy in retroperitoneum group.
Results: In excluding retroperitoneum group, median follow-up after radiotherapy was 36 months while 26 months in retroperitoneum group. In excluding retroperitoneum group, 3 and 5 year general survival rates (G.S) were determined respectively 75% and 69%, disease-free survival rates (D.F.S) were 56% and 51%, local control rates (L.C) were 70% and 65%. On multivarian analysis: Surgical margins remained statistically significant for G.S ($p = 0.004$), DFS ($p < 0.0001$) and L.C ($p = 0.01$). Also histological grade was statistically significant in D.F.S ($p = 0.03$). In L.C., presenting symptome ($p = 0.04$; pain worse than swelling) was the other factor changing the prognosis. In retroperitoneal region group, 3 and 5 year G.S. rates were determined respectively 69% and 69%, D.F.S. rates were 52% and 52%, L.C. rates were 61% and 61%. On multivariate analysis: In G.S., operation status remained statistically significant ($p = 0.02$). In D.F.S gender ($p = 0.003$; better in women) and operation status ($p = 0.01$) were statistically significant factors. In L.C. only gender ($p = 0.02$) was the factor changing the prognosis.
Conclusion: Our results are supporting the literature which was not much hopeful for this rare kind of disease. It is also interesting that, gender was the most important prognostic factor for both D.F.S. and L.C. in retroperitoneal region group.

9425 POSTER

Administration of 24-hour intravenous infusions of trabectedin (Yondelis®) every 3 weeks in ambulatory patients with mesenchymal tumors via the disposable elastomeric pump Baxter LV10: a feasible, convenient, effective and patient-friendly palliative treatment option

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Background: Patients (pts) with sarcoma whose disease progresses after standard chemotherapy have poor outcome. In this setting, the DNA-transcription-interacting cytotoxic agent trabectedin (TRA) is efficacious and marketed in Europe. It is administered as 24-h i.v. infusion q3w with steroid co-medication. To overcome the inconvenience of hospitalization for drug delivery TRA is now given in Leuven via disposable elastomeric pumps, which facilitate ambulatory treatment and are compatible with the drug.
Material and Methods: Heavily pre-treated pts with sarcoma were offered chemotherapy with TRA 1.5 mg/m^2 as 24-h i.v. infusion via port catheter, either during hospitalization using electronic pumps or as outpatients using the Baxter LV10 disposable pump (drug dissolved in 267 ml NaCl 0.9%). Co-medication consisted of antiemetics and dexamethasone 2x4 mg days −1, 1, 2, 3.
Results: Between 09/07−12/08 28 pts were treated, and 21 (75%) elected outpatient therapy (9 F, 12 M, med. age 49 yrs, range 19−68). Common diagnoses included leiomyo- (5), lipo- (4), synovial (2) and myxofibrosarcomas. Pts had previous primary surgery (17), adjuvant radiotherapy (4) and surgery for relapse/metastasis (7). They had local relapse (2), distant metastasis (12) or both (7) when starting TRA, 19 had received previous chemotherapy with a med. number of 2 prior lines (range, 0−5). We administered 130 cycles of TRA in 21 pts, with a med. number of 3 cycles/patient (range, 1−24). Dose reductions were done in 60 cycles, mainly due to laboratory events. Best response (RECIST) was 4 confirmed PR, 6 SD, 11 PD. Grade 3/4 (CTC) AEs were limited to one case each of haemorrhage and lung embolism, other AEs were in line with published TRA experience. One port catheter contamination required replacement, one catheter tip thrombosis occurred and one extravasation due to needle dislocation was observed.
Conclusions: Outpatient administration of TRA as 24-h infusion via port catheters using Baxter LV10 pumps is preferred by 3/4 pts, is feasible, safe, efficacious and cost-efficient and should be considered routine practice in this clinical setting.

9426 POSTER

Trabectedin 3-hour infusion every 3 weeks in pre-treated advanced sarcoma patients: a compassionate-use administration experience

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Background: Limited data are available on the benefits of Trabectedin (Yondelis®; T) among compassionately-treated outpatients with sarcoma.
Material and Methods: A retrospective evaluation of safety and efficacy of T administered as 3-h infusion every 3 weeks (q3wk) to pre-treated sarcoma patients (pts) was done in a compassionate-use programme.
Results: A total of 104 pts were analysed. Baseline characteristics were: 77 (78%) had soft tissue sarcoma (STS) (leiomyosarcoma 23%, liposarcoma 22%, synovial sarcoma 10%, fibrosarcoma 9%, and malignant fibrous histiocytoma 8%), 25 (26%) had bone sarcoma (osteosarcoma 48%, Ewing sarcoma 32% and chondrosarcoma 20%) and 2 had gastrointestinal stromal tumours. Median (*m*) age was 40 yr, 83% had PS 0−1, 86% with metastatic disease, 40% had grade (G) 3 tumours, 34% had bulky disease; 81% received prior surgery and 53% prior radiotherapy. All received prior chemotherapy (anthracyclines 99% and ifosfamide 89%) with a *m* number of lines: 2 (1−9), and 32% of pts had received $\geqslant$ 3 lines. The *m* initial starting dose was 1.3 mg/m^2 (0.9−1.7); *m* number of cycles per pt: 2 (1−22); 16% received $\geqslant$6 cycles; 54% of pts had cycle delays and 32% underwent dose reduction (mainly due to non-haematological toxicity). Safety: G 3/4 haematological toxicities were neutropenia 42%, febrile neutropenia 7%, thrombocytopenia 27% and anaemia 17%. ALT and AST elevations occurred in 69% and 55% of pts, respectively. Most

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 ± 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.

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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,