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.

Results: A successful collaboration has been initiated. To 31-Mar-2007, accrual was on target, with 499 patients registered within 2 years from 199 institutions in 12 countries; including 88 patients so far in 2007. Approximately 80% are www.euramos.org; details about the ECT-program at www.esf.org.
Conclusions: International trials in rare diseases are practicable with the appropriate funding, planning and support. EURAMOS1 may serve as a model for a successful multinational clinical trial in times of increasing economic and regulatory pressure. It has the quickest accrual rate of any osteosarcoma trial ever and in 2007 should become the largest osteosarcoma study ever conducted.
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7522 POSTER

Postoperative experience in patients with metastatic GIST are similar in patients while on sunitinib or imatinib

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Introduction: Sunitinib malate (SU) is now standard therapy for pts with metastatic gastrointestinal stromal tumor (GIST) resistant or intolerant to imatinib mesylate (IM). A theoretical concern is that inhibition of multiple receptor tyrosine kinases (RTKs) by SU could impair healing after cytoreductive procedures. We reviewed our experience to compare the spectrum of postoperative complications after SU vs. IM therapy.
Materials and Methods: Records from all pts who underwent cytoreductive surgery while enrolled in phase II/III SU trials at our institution were compared with records from those who underwent similar surgery while on IM. Perioperative SU dosing and complications after surgery and after resumption of SU were recorded. Complications related to healing included wound/fascial dehiscence, anastomotic leak, and fistula. Complications not attributed to wound healing included hemorrhage, abscess, seroma, and ileus.
Results: 188 pts with metastatic GIST were treated with SU after developing IM resistance or intolerance. 72 pts underwent 81 operations for disease resection (breakdown can be seen in table). SU was stopped 5 days (median; range 0–26) prior to surgery and resumed 33 days (median; range 12–183) after surgery and 20 days (median; range 7–178) after hospital discharge. Resumption of SU treatment generally coincided with the first postoperative clinic visit (see table for total complications). In the two SU pts with wound-healing complications (dehiscence, fistula, or leak), treatment was stopped 9 and 22 days prior to surgery, respectively. No wound-healing complications were noted among the 18 pts who stopped SU.

	Sunitinib malate (N = 26)	Imatinib mesylate (N = 46)	P-value
Gender, n (%)			NS
Men	16 (62)	28 (61)	
Women	10 (38)	18 (39)	
Total procedures, n	28	53	
Complications after surgery, n (%)			
Dehiscence/fistula/leak	2 (7)	4 (8)	NS
Intraabdominal hemorrhage/abscess/seroma	6 (21)	6 (11)	NS
Ileus	2 (7)	6 (11)	NS
Other	4 (14)	4 (8)	NS
Complications after resumption of drug, n (%)			
Wound healing/fistula	1 (4)	1 (2)	NS
Abscess/seroma	1 (4)	2 (4)	NS
Total procedures with complications, n (%)	14 (50)	20 (38)	NS
Total number of complications, n	17	23	

Conclusions: There were no differences in wound-healing complications following cytoreductive procedures between pts with metastatic GIST on SU or IM therapy, despite the broader spectrum of RTK inhibition by SU. Our current practice is to continue SU until 1–2 days prior to surgery and to resume SU at the first postoperative visit.

7523 POSTER

High-dose chemotherapy and autologous peripheral blood stem cell transplantation after the completion of long-lasting St. Jude Hospital protocol: early results of a pilot study

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Background: Ewing sarcoma has a worse prognosis in metastatic stage. The efficacy of high-dose chemotherapy and autologous peripheral stem cell transplantation is not well determined in this group of patients. In this study, we investigated the effectiveness of high-dose chemotherapy and autologous peripheral stem cell transplantation in metastatic patients after the completion of long-term St. Jude Hospital treatment protocol, as well as the toxicity profile.
Materials and Methods: Seven patients with metastatic ewing sarcoma who achieved 41-week St. Jude hospital long-term treatment protocol were included in the study. Among these patients, 5 patients (72%) achieved initially a complete response after the treatment protocol, 1 patient (14%) achieved a partial response, and 1 patient (14%) had progressive disease. G-CSF was applied on a dose of 10 microgram/kg/day for four days to mobilize the stem cells. Apheresis was done on the fifth day after G-CSF application. High-dose ICE (ifosfamide 12 g/m2, etoposide 1.2 g/m2, carboplatine 1.2 g/m2) chemotherapy was given after 7 to 10 days after stem cell apheresis.
Results: The median age of patients was 20 (range: 5−28) years. Tumor localization site was the extremities in 6 cases and in the other patient the tumor originated from the pelvis. Six patients (86%) underwent surgical resection, and radiotherapy was applied in all patients (100%) during St.Jude treatment protocol. Median time to stem cell transplantation from the last chemotherapy was 5.5 months. After the stem cell transplantation 5 patients had progression (1 patient developed metastasis in liver and 4 patients in lung). Two other patients had stable disease. Three patients have died in the second, third and fifth months of the transplant, respectively. The toxicities during St. Jude treatment protocol were myelosuppression in 4 cases, transient liver toxicity in 1 case, and 4 patients have required G-CSF and erythrocyte transfusions. During high-dose chemotherapy grade III/IV toxicities were leucopenia (50%), anemia (45%), trombocytopenia (36%) and neutropenic fever (36%). No patient has died due to high-dose chemotherapy. 5-year survival was calculated as 30%.
Conclusions: In conclusion, autologous peripheral stem cell transplantation in metastatic patients with Ewing sarcoma treated initially with 41-week long-lasting treatment protocol may provide partial benefit in terms of survival and tolerable toxicity. Large randomized studies with high number of patients may demonstrate the efficiency of high-dose chemotherapy together with stem cell transplantation for consolidation or salvage treatment in patients with metastatic Ewing sarcoma.

7524 POSTER

ZIO-201, isophosphoramide mustard in advanced sarcoma

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Background: ZIO-201, a bi-functional DNA alkylator, is the active metabolite of ifosfamide (IFOS). IFOS and cyclophosphamide (CPA) are widely used anti-cancer drugs. Both are pro-drugs and need to be metabolized for activity. Their clinical use is limited by toxicities associated with metabolites unrelated to DNA-alkylation and by development of resistance conferred by decreased pro-drug activation. ZIO-201 has broad activity against human sarcoma cell lines in vitro and in human xenograft models. Importantly, it is active in IFOS and CPA-resistant human osteosarcoma cell lines and xenografts.
Methods: Phase 1/2 study to evaluate safety, pharmacokinetics (PK), maximum tolerated dose (MTD), dose-limiting toxicity (DLT) and efficacy in patients with advanced sarcoma. Starting dose of 590 mg/m^2/day based on a Phase 1 study in patients with advanced malignancy; however dose was reduced and recommended Phase 2 starting dose was 413 mg/m^2/day ZIO-201 was given IV daily for 3 consecutive days every 21 days with pre-specified dose modifications between cohorts.
Results: 10 Patients with advanced sarcoma [synovial sarcoma (N = 2); leiomyosarcoma (N = 2); fibrosarcoma (N = 1); malignant fibrous histiocytoma – MFH (N = 1), liposarcoma (N = 1), Ewing sarcoma (N = 1) and others (N = 2)] were treated; 4 received 590 mg/m^2/day and 6 received