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

413 mg/m^2/day. Median age was 43 y (range 25–67 y). All had ECOG PS < 2. 5 patients received IFOS previously with sarcoma-progression. MTD was 413 mg/m^2/day and DLT proximal renal tubular acidosis (PRTA); no hemorrhagic cystitis or CNS-toxicity. At the Phase 2 recommended dose of 413 mg/m^2/day, 2 of 5 evaluable patients had stable disease. One patient with a liposarcoma had a 25% reduction in the tumor burden at 6 weeks, and a second patient with chondrosarcoma had stable disease for 5 cycles. Both these patients are ongoing.
Conclusions: Based on current clinical experience ZIO-201 has potential for the treatment of sarcoma including patients with IFOS-resistance. MTD is 413 mg/m^2/day; DLT is PRTA. There was no hemorrhagic cystitis; despite not using mesna nor was there CNS-toxicity. Bone marrow toxicity was only modest. Plasma levels at MTD exceed the IC50 of human sarcoma cells in vitro. The study continues to accrue patients.

7525 POSTER

Treatment of malignant sacral tumors except chordoma

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Background: Treatment of malignant sacral tumors represents one of the most difficult problems in musculoskeletal oncology. Because of the rarity of the disease and complicated anatomy (neurological and structural) of the sacrum there is no established method of treatment for these tumors and no comprehensive analysis has been reported so far besides chordoma. With these considerations in mind, this study was undertaken to ascertain the prognosis of patients with sacral tumors in order to help to define the role of various treatment methods in these rare malignancies.
Materials and Methods: Thirty-three patients with primary sacral tumors (excluding chordoma) treated in our institutes between 1987 and 2006 were retrospectively analyzed. There were 19 males and 14 females ranging in age from 10 to 76 years (median 35 years). The histologic diagnosis was Ewing's sarcoma/primitive neuroectodermal tumor (ES/PNET) in 8, chondrosarcoma in 8, osteosarcoma in 3, giant cell tumor (GCT) in 10 and other malignant tumors in 4. Tumors ranged in size from 4 to 18 cm (median 8 cm). Four patients had metastases at the time of diagnosis. Surgical excision of the tumor was performed in 12 patients: resection in 5 (margin negative 2, positive 3) and curettage in 7 (all for GCT). Radiotherapy (40−70 Gy) was applied in 20 patients (including 10 carbon ion radiotherapy). Chemotherapy was used in 16 patients.
Results: At the time of last follow up (median 36 months), 18 patients were disease free, 5 were alive with disease, and 10 had died. Thirteen patients (39%) had developed a local recurrence (ES/PNET 2, chondrosarcoma 5, osteosarcoma 2, GCT 3, other 1) at a median time of 14 months. Carbon ion radiotherapy could achieve a local tumor control in the majority of ES/PNET and approximately one half of chondrosarcoma or osteosarcoma patients. Ten patients (30%) developed distant metastases (ES/PNET 3, chondrosarcoma 2, osteosarcoma 2, others 3) at a median interval of 16 months. The 3- and 5-year overall survival rates of the patients (excluding GCT) were 55% and 38%, respectively. All surviving patients could walk with/without short leg orthosis.
Conclusion: The prognosis of patients with malignant sacral tumors remains poor despite modern multimodality treatment. Given the morbidity and poor functional results of the complete or high sacral amputation, carbon ion radiotherapy could be a valid alternative for these difficult-to-treat diseases.

7526 POSTER

Adjuvant radiotherapy for retroperitoneal soft tissue sarcoma

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Background: To evaluate clinical outcomes and prognostic factors of retroperitoneal soft tissue sarcoma treated with postoperative radiotherapy
Materials and Methods: The records of 24 patients with retroperitoneal soft tissue sarcomas who underwent postoperative radiotherapy between 1985 and 2003 were analyzed. Median follow-up duration was 71 months (range, 7–240 months). Twenty-two patients presented with primary disease and two patients presented with recurrent disease. Liposarcoma and leiomyosarcoma represented 75% of the tumors. Eighty-nine percent of the tumors were high grade (grade 2 or 3). Median tumor size was 13.5 cm (range, 3−50 cm). Complete excision was achieved in 68% of patients. Radiation dose ranged from 45 to 63 Gy (median, 50.4 Gy) with conventional fractionation.
Results: The 5-year overall, local recurrence-free, and distant metastasis-free survival rates were 67%, 57%, and 70%, respectively. Twelve and nine patients experienced local recurrences and distant metastases, respectively. Most common site of distant metastases was liver. On univariate analysis, adjacent organ invasion and age >60 years were significant risk factors predicting poor overall survival. Adjacent organ invasion remained significantly associated with a higher risk of death by multivariate analysis. An interval between surgery and the start of radiotherapy of >30 days was an adverse risk factor for local recurrence by univariate and multivariate analyses. Except one grade 3 diarrhea, no patient suffered grade 3 or higher complication.
Conclusion: Our results were comparable to those of reported. Adjacent organ invasion was a predictor of poor survival and recurrence. Delayed radiotherapy may compromise local control of retroperitoneal soft tissue sarcoma.

7527 POSTER

Postoperative radiation therapy in high-risk pigmented villonodular synovitis

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Background: Pigmented villonodular synovitis (PVNS) is an uncommon proliferative disorder, and appears pathologically thickened, reddish-brown synovium with numerous villous projections. It affects synovium, bursa, and tendon sheath, and is able to invade muscle, tendon, bone, and skin. The type of PVNS is classified into localized (LPVNS) and diffuse (DPVNS). Incompletely resected LPVNS or DPVNS has relatively high local recurrence rate after surgery, although the optimal treatment is microscopic or open synovectomy. This study observed the local recurrence rate and treatment-related complication after postoperative radiation therapy in patients with high-risk, incompletely resected PVNS.
Materials and Methods: Twenty-two patients treated with surgery and postoperative radiation therapy between March 1999 and September 2004 were reviewed. All patients have high-risk local recurrence factors which was DPVNS or incompletely resected LPVNS. Median age was thirty-eight years (range: 10−64 years) and 15 patients (68%) were female. Involved site of joint were Knee in 19 patients, ankle in 2, and hip in 1 patient. Seventeen (77%) patients had DPVNS, and seven (32%) patients had a recurrent disease in same joint. Irradiated dose was 20 Gy in 12 patients (55%), 26 Gy in 2 (9%), and 34 Gy in 8 patients (36%). Radiation field encompassed 5 cm margin beyond tumor bed or surgical sites in all treatment. Follow-up with MR or ultrasound imaging was done in 13 patients, and the other 9 patients were evaluated by physical exam or simple X-ray on follow-up.
Results: Median follow-up time was 24 months, and its range was 13−64 months. Four (18.2%) patients showed local recurrences in radiation field. Time to recurrence was 1 year in 2 patients, and 43, 59 months in the other 2 patients. Two patients received salvage operation or re-radiation therapy. Among 18 patients without local recurrence, fifteen (83.3%) patients had no complaint and good joint function after treatment, one patient had mild stiffness in irradiated knee joint, and the other two patients had mild pain.
Conclusions: Postoperative radiation therapy to high-risk pigmented villonodular synovitis is an effective treatment for local tumor control without severe complication.