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

C. Raut[1], J.A. Morgan[2], M.T. Quigley[2], S. George[2], A.J. Wagner[2], G. Demetri[3], M.M. Bertagnolli[2]. *[1]Dana-Farber Cancer Institute/Brigham and Women's Hospital, Surgical Oncology, Boston MA, USA; [2]Dana-Farber Cancer Institute/Brigham and Women's Hospital, Medical Oncology, Boston MA, USA; [3]Dana-Farber Cancer Institute/Harvard Medical School, Medical Oncology/Solid Tumor Oncology, Boston MA, USA*

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

A.S. Ataergin[1], M. Ozturk[1], M. Turan[2], A. Ozet[1], F. Arpaci[1], M. Beyzadeoglu[3], K. Oysul[3], F. Kilicli[1], S. Komurcu[1], B. Ozturk[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: 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

R. Chugh[1], R. Benjamin[2], S. Chawla[3], J. Heaton[1], B. Schwartz[4]. *[1]Univ of Michigan Health Syst, Ann Arbor MI, USA; [2]MD Anderson Cancer Center, Houston TX, USA; [3]Santa Monica CA, USA; [4]Ziopharm Oncology, Charlestown MA, USA*

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