(14–72), median (WHO) PS = 1 (0–2). Pre-treatment: surgery 34/48, chemotherapy 1/48, radiotherapy 15/48, stage of disease IIIB = 17%, IV = 83%. Median number of cycles (in 43 pts evaluable for response) = 6 (range 2–8), median cumulative EPI dose = 740 mg/m^2 (range 290–1280 mg/m^2). We observed 3 CR and 13 PR (37%) [95% CI, 23%–51%]; 14 NC (33%); 13 PD (30%). Responses were observed in 6/11 liposarcoma, 2/6 leiomyosarcoma, 1/5 MFH, 2/8 synovial sarcoma, 1/3 malignant schwannoma, 1/3 fibrosarcoma, 1/2 stromal sarcoma, 2/4 other types. Median duration of response was 10 months (range 4–38+). Median time to progression was 9 months (range 3–42+). Median overall survival was 14 months (range 3–42+) with a significant difference between responding (17 months) and progressive pts (6.5 months). The most important side effect was myelotoxicity with leukopenia occurring in all patients (G4 38%), thrombocytopenia in 36% (G1–G2 18%) and anemia in 72% (G1–G2 53%) of the pts. In 11/43 pts (26%) EPI dose was reduced because of myelotoxicity. Neutropenic fever occurred in 28% of the pts. Stomatitis was recorded in 36% of the pts and N/V (G3) in 6% of the pts. Cardiotoxicity was monitored in 24 pts by radionuclide angiography. Only 3/24 pts experienced a $\geqslant$20% decrease in left ventricular ejection fraction at cumulative doses of 880 mg/m^2, 960 mg/m^2 and 1280 mg/m^2. Clinical cardiotoxicity was not observed. HD-EPI is an effective and reasonably well tolerated treatment in advanced STS. In comparison to our previous study a dose-response effect has been observed at EPI doses of 160 mg/m^3. The accrual of pts continues to better define the effectiveness and the toxicity of this treatment.

862 POSTER

CD3 NEGATIVE LARGE GRANULAR LYMPHOCYTES RECOGNIZE AN IMMUNOGENIC DETERMINANT ASSOCIATED WITH THE 72 KD HEAT SHOCK PROTEIN (HSP) ON HUMAN SARCOMA CELLS

G. Multhoff, C. Botzler, M. Wiesnet, W. Wilmanns, R.D. Issels
GSF-Institut für Klinische Hämatologie and Medizinische Klinik III, Klinikum Großhadern, D-81366 München, Germany

Traditionally, heat shock proteins (HSP) are believed to be located intracellularly, where they perform a variety of chaperoning function. However, recent publications have demonstrated that under certain circumstances malignant cell types express HSP on the cell surface. Our studies confirm this finding and correlate HSP72 cell surface expression, induced by nonlethal heat shock, with increased tumorigenicity against CD3$^-$ natural killer cells (NK). A monoclonal antibody (mAb, RPN1197) directed against the major heat inducible 72 kD heat shock protein (HSP72) binds to the cell surface of tumor cells (i.e. human Ewing's sarcoma cells or osteosarcoma cells), but not to normal cells (i.e. PBL, fibroblasts, PHA blasta, B-LCL) after single nonlethal heat shock (41.8°C, 200 min) followed by a recovery period at 37°C (4 h). Despite a decrease in the MHC class I cell surface expression after heat shock a marked increase (2-fold) in tumorigenicity as compared to untreated tumor cells was found. Analysis of cytotoxic activity of CD3$^-$ large granular lymphocytes (NK cells), CD3$^+$ MHC restricted CTL and unseparated effector cells in a cell mediated lympholysis assay (CML), demonstrated that the CD3$^-$ NK effector cell population and not the GD3$^+$ CTL population, is responsible for the recognition of heat shocked tumor cells. By antibody inhibition (using this HSP72 specific mAb, RPN1197) an immunogenic HSP72 determinant, which is expressed only on the cell surface of tumor cells after nonlethal heat shock could be determined as the relevant recognition structure for CD3$^-$ NK cells. As a control, blocking of MHC class I restricted recognition (using either MHC class I specific mAb W6/32 on the target cells or a/β TCR WT31 on effector cells) had no inhibitory effect on the lysis of heat shocked tumor cells. In summary, our data indicate that CD3$^-$ NK cells recognize a heat inducible HSP72 related immunogenic epitope, on the cell surface of sarcoma cells, but not on normal cells.

Supported by grant M90/91-Isl from the Deutsche Krebshilfe and EC-Project CHRX-Ct93-0260

863 POSTER

CLINICAL APPLICATIONS OF FDG POSITRON EMISSION TOMOGRAPHY IN PATIENTS WITH SOFT TISSUE SARCOMA

O.E. Nieweg, R.J. van Ginkel, J. Pruim, H.J. Hoekstra, A.M.J. Paans, A.C. Kole, W.M. Molenaar, W. Vaalburg, H. Schraffordt Koops
University Hospital, Groningen, and The Netherlands Cancer Institute, Amsterdam, the Netherlands

Various applications of positron emission tomography (PET) were studied in patients with soft tissue sarcoma: depiction of primary and recurrent lesions, determination of malignancy grade and evaluation of response to regional isolation perfusion.

Twenty-nine patients with various types of soft tissue sarcoma were studied, 17 with a primary tumor and 12 patients with a local recurrence. The tumor size ranged from 1.0 to 31 cm.

An IV dose of 370 MBq ^{18}F-fluoro-deoxy-D-glucose (FDG) was administered. PET studies were performed in a dynamic and a "whole body" mode using a Siemens ECAT 951 camera.

All 17 primary tumors and 11 of the 12 recurrent sarcomas were well visualized on the PET studies. The location of the recurrent lesions was clearly depicted in the presence of surrounding scar tissue and fibrosis.

The glucose metabolic rate in the lesions was found to increase with increasing malignancy grade ($P < 0.05$).

The decrease in glucose metabolic rate after TNF perfusion (20 patients) was found to provide information about the tumor response.

In summary, several clinical applications of PET with FDG were established in patients with soft tissue sarcoma.

864 POSTER

COMBINED RADIATION AND SURGERY FOR MALIGNANT FIBROUS HISTIOCYTOMA OF SUBCUTANEOUS TISSUE

I.J. Spiro, H.D. Suit, J. Fanberg, A.E. Rosenberg
Massachusetts General Hospital, Boston, MA, U.S.A.

Materials and Methods: The records of 21 patients treated with surgery and radiation for malignant fibrous histiocytoma (MFH) of subcutaneous tissue were identified.

Results: The majority of patients with subcutaneous MFH (83%) showed an extremely infiltrative growth pattern, defined as >0.2 cm from the main mass. These tumors frequently showed positive surgical margins (60%) after initial resection and frequently required reexcision and skin grafting. Two local failures were reported, one of these eventually developing distant failure. Two other patients eventually developed distant failure without evidence of local failure.

Conclusions: Subcutaneous MFH show a highly infiltrative behavior, frequently showing positive margins after initial surgery. Contrary to prevailing opinion these tumors are locally aggressive and can display local and distant recurrence.

865 POSTER

GRAFTING DISTAL ARTICULAR ENDS OF THE FEMUR FOR MALIGNANT BONE TUMORS

G.M. Vedzizhev
Medical Radiological Research Center of RAMS, 249020 Obninsk, Russia

Management of malignant bone tumors of distal ends of the femur with osteoplasty remains a complicated problem. We evaluated results of limb-salvage operations for the last 3 years. In 20 patients (12 females, 8 males) aged 4.5 to 45 years operations were performed. There were 11 osteogenic sarcomas, 3 malignant osteoblastomas, 3 fibrosarcomas, 2 parosteal sarcomas and 1 Ewing's sarcoma. 5 patients received preoperative radiation therapy and 15 patients—polychemotherapy. 11 patients underwent grafting by an analogous cadaveric allograft and 9 children by a boiled down autograft. Bone fragments were connected using a set of instruments proposed by us and fixatives. Most patients achieved good results.

866 POSTER

COMBINATION OF DOXORUBICIN/IFOSFAMIDE ± G-CSF IN ADULT METASTATIC SOFT TISSUE SARCOMA (STS)

H.J. Weh, M. de Wit, D.K. Hossfeld
Department of Oncology and Hematology, Medical University Clinic, 20246 Hamburg, Germany

Our present protocol for adult metastatic STS comprises the combination of doxorubicin 30 mg/m^2/days 1 + 3 and ifosfamide 3 g/m^2/days 1–3 given every 3 weeks. The first course of treatment is given without support of G-CSF. In cases of leukopenia grade 4 after any cycle the following cycles are given with G-CSF 5 μg/kg/day. So far, 124

courses of chemotherapy have been administered to 35 pts. After the first course 18/35 pts developed leukopenia grade 4 and 7 pts had non fatal febrile episodes necessitating antibiotic therapy. These 18 pts received additional 54 courses of chemotherapy followed by G-CSF. Although 24 episodes of leukopenia grade 4 were noticed, only one patient developed a febrile infection. 17/35 pts continued treatment after the first course without support of G-CSF. Four of them developed leukopenia grade 4 after the second and third course, respectively, so that only 13 pts received all cycles of chemotherapy without G-CSF. None of several clinical parameters, such as pts' sex and age, performance status, localization of metastases or WBC before treatment could predict the probability of development of leukopenia grade 4. So far, response rates are: CR 6%, PR 24%, SD 38%, and PD 32%. *Conclusion:* The above described regimen is a hematotoxic combination. However, it can be given to about 30% of adult pts with metastatic STS without support of G-CSF. With regard to the high cost of G-CSF we believe that it is justified to administer the first course of this chemotherapy without support of G-CSF. However, under these conditions, the immediate initiation of antibiotic treatment in cases of fever must be guaranteed.

867 PUBLICATION

SUPERFICIAL SOFT TISSUE SARCOMAS OF THE ADULTS

L. Cany, E. Stöckle, J.M. Coindre, A. Ravaud, G. Kantor, N.B. Bui
Institut Bergonié, 180, rue de Saint-Genès, 330746 Bordeaux Cedex, France

A series of 105 consecutive patients with superficial soft tissue sarcomas was analysed to assess the evolution of these tumors. There were 56 men and 49 women, aged 16 to 80 years (median: 56.4 years). Tumor localizations were 59 limbs (56.2%) and 41 non-limbs. The median tumor size was 3 cm (range 1 to 15 cm). Histological types were mainly malignant fibrous histiocyto-fibromas (n = 39 / 36.8%), leiomyosarcomas (n = 20 / 18.9%), dermatofibrosarcomas protuberous (n = 8 / 7.5%). According to the FNCLCC grading, tumor grade was: grade 3 = 24, grade 2 = 54, grade 1 = 28.

With a median follow-up of 112 months (range 19 to 321 months), the 5-year overall and disease-free survival were 75% and 46%. In monofactorial analysis, tumor grade is the only predictive factor for overall survival (grade 1 vs grade 2: $P = 0.02$; grade 2 vs grade 3: $P = 0.0002$), and for metastasis-free survival (grade 1 vs grade 2: $P = 0.05$; grade 2 vs grade 3: $P = 0.0006$). For grade 2 tumors, metastases occurred only after a deep, local recurrence. Age, tumor size, tumor localizations were not statistically significant. For the local relapse-free survival, tumor size (<5 vs $\geqslant 5$ cm) was the only predictive factor ($P = 0.0006$).

868 PUBLICATION

IMPACT OF LOCAL RECURRENCES IN SOFT TISSUE SARCOMA SURGERY

J. Høie, Ø.P. Solheim, A.E. Stenwig
Norwegian Radium Hospital, 0310 Oslo, Norway

Primary surgery in soft tissue sarcomas may be a dilemma between saving functions, abstain of mutilation and the potential of local recurrence. *Material:* 394 consecutive patients treated before 1990 have been analyzed.

Results: 100 patients presented with 150 recurrences; 79 patients with one recurrence only. In these 79, distant spread were seen concomitant with the local recurrence in 27, another 25 patients are free of disease following treatment of their recurrence, in 15 wide primary excisions were impracticable, and 6 patients were above their 80-ties. In 6 patients only, more extensive primary surgery should be advocated. In 7 patients with 4 to 8 episodes of recurrence, 2 died of distant disease, 1 of the local disease and 4 are free of disease. *Conclusion:* impact of local recurrence is moderate and may be accepted in lieu of mutilating surgery.

869 PUBLICATION

SUCCESSFUL AGGRESSIVE CHEMOTHERAPY IN PATIENTS WITH CHONDROSARCOMA: A REPORT OF FOUR CASES

P. Reichardt[1], S. Lentzsch[1], P. Hohenberger[2], B. Dörken[1]
[1]*Free University of Berlin, University Medical Center Rudolf Virchow, Robert-Rössle-Hospital, Department of Medical Oncology*
[2]*Department of Surgery, D-13122 Berlin, Germany*

Chondrosarcoma (CS) is uniformly reported to be resistant to any chemotherapy. A possible exception may be mesenchymal CS where occasional responses can be seen. Still the literature is scarce.

We report 4 patients treated with aggressive chemotherapy consisting of ifosfamide 2.5 g/m^2/day days 1 to 5, epirubicin 45 mg/m^2/day days 2 and 3 and Filgrastim 5 μg/kg/day s.c. days 6 to 15.

The first pt., a 35 ys. old female with a local recurrence and multiple lung metastases of a mesenchymal CS showed a CR of all detectable tumor manifestations after 6 cycles and is disease free for 14+ month. The second pt., a 28 ys. old male with multiple lung mets. of a CS is in continuous complete remission for 3+ month. Two additional patients with multiple lung mets. of a CS showed a stable disease for 13 and 3 months respectively after completion of 4 cycles. Both patients were put on oral chemotherapy with trofosfamide and are still under treatment.

We conclude that in selected cases of CS aggressive treatment should be considered, especially in younger patients.

870 PUBLICATION

DESMOID TUMORS (AGGRESSIVE FIBROMATOSIS): RETROSPECTIVE STUDY

O. Sousa, L. Carvalho, I. Silva, M. Bento, E. Vieira
Department of Radiation Oncology, Instituto Português de Oncologia 4200 Porto, Portugal

Although benign, desmoid tumors are locally aggressive neoplasms which infiltrate adjacent tissues, resulting in a high incidence of local recurrence after conservative resection. Between 1982 and 1993, 10 female and 5 male patients with histologically confirmed desmoid tumors were referred to Instituto Português de Oncologia—Porto. Age ranged from 12 to 47 years, with 2 newborn patients. Sites of disease included head and neck (n = 5), shoulder girdle (n = 3), chest wall (n = 2), abdomen (n = 2), extremities (n = 2) and back (n = 1). Patients were treated with surgery alone (n = 3) or surgery plus radiation (n = 12). Ten patients underwent radiation therapy for uncertain, positive margins or subtotal resection and 2 received planned postoperative radiation (microscopically negative margins), the majority being treated to a tumor dose of 40–70 Gy. With a medium follow up of 4.5 years, 14/15 patients are without evidence of disease and one died with progressive multicentric disease. In the irradiated group, 2 patients with infield recurrence and another with marginal recurrence were successfully treated with surgery. In summary, we believe that moderate doses of radiation can improve local control rates minimal long-term effects.

871 PUBLICATION

LOW EFFICACY OF 1 HOUR INFUSION-HIGH DOSE IFOSFAMIDE (IFO) IN PREVIOUSLY PRETREATED SARCOMA

M. Tubiana-Hulin, F. Cvitkovic, F. Lokiec, L. Bozec, A. Goupil, M. Janvier, F. Turpin, J. Rouëssé
Centre René-Huguenin, Saint-Cloud, France

Following Antman's report (Sem Onc 1990; 17: 7–15) underlining a better efficacy for fractionnated bolus Ifo infusion modality than the 24 h continuous infusion, as treatment in relapsing sarcoma patients, in October 93 we began a phase II study of high dose (HD) Ifo at 4 g/m^2/d on 3 consecutive days (12 g/m^2/cycle) given over 1 hour/d with Mesna (doses $\times$ 1.5) every four weeks until progression. Twelve patients (pts) were entered, their characteristics as follows: median age 40 ys (18–62); sex 5 M/7 W; PS $\leqslant$ 1 12/12 pts; histologic types: bone sarcoma (sarc) 3 (2 osteosarc, 1 fibrosarc), soft tissue sarc 9 (synovialosarc 3, liposarc 2, other types 4). Ten pts had metastatic disease and 2 a locally advanced inoperable sarcoma. All pts were pretreated with chemotherapy, (1 regimen, (rg) 6 pts, 2 reg, 6 pts), the MAID regimen in 7 of them. Four/9 pts treated previously with intermediate dose of Ifo 9 g/m^2/cy (IDIFO) had responded to it.

Results: 35 cycles (cy) were administered, median number of cy/pt = 2 (1–6). All pts were evaluable for response. The only PR (8 weeks duration) was a previous complete responder to IDIFO. Of the 3 minor responders observed (median duration 3 months), one had previously responded to IDIFO. Seven pts had disease progression and there was one stabilisation. Toxicity/cy included: 7 febrile neutropenia episodes during the 1st cy, 2 of them despite G-CSF prophylaxis; all following cycles were administered with G-CSF; 1 grade 3 and 1 grade 2 thrombopenia, 1 grade 3 renal insufficiency, 1 grade 2 haemorrhagic cystitis. CNS toxicity related to treatment was seen in 1 cy (1 transient confusion). There was no dose modification, and no toxic death occurred. All treatment discontinuations were caused by progressive disease, or patient refusal (1 pt).

Conclusion: Our experience with HDIFO (12 g/m^2/cycle) contrasts with other reports showing a good efficacy of HDIFO in refractory sarcomas (Brain ASCO 95 A1641). Our series consists of pts pretreated