(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

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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.

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863 POSTER

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

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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

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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

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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)

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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