Methods: From 1993 until 1996 17 patients (pts.) with primary (N = 11); recurrent (N = 4) or metastatic (N = 2) soft tissue sarcomas were treated with preoperative concurrent radio-chemo-therapy (RCT). Sarcomas were localized in the extremities (N = 10); the trunk (N = 4); head and neck region (N = 2) and in the penis (N = 1). Chemotherapy consisted of ifosfamide 1.5 mg/m^2 and mesna (d 1–5 and 29–33) as well as adriamycin 50 mg/m^2 (day 2 and 30) Accelerated-hyperfractionated radiotherapy (RT) was applied in 2 fractions/d of 1.5 Gy up to 56 to 60 Gy (day 1–45; after 30 Gy 1 week RT-break). After 4–8 weeks residual tumour mass was excised according to the guidelines of oncological surgery.

Results: Following neoadjuvant RCT 16/17 patients were treated by surgery. All the 16 pts had a histologically complete resection (R0). In 4/16 pts (25%) there was no vital tumour in the speciment. Limb sparing surgery was possible in 7/10 pts. Myelosuppression was most prominent with leucopenia grade 4 in 6/17 and grade 3 in 4/17 pts; thrombocytopenia in grade 3 in 2/17; grade 4 in 1/17. Skin toxicity was grade 3 in 5/17 and grade 4 in 1/17.

Conclusion: Preoperative RCT is feasible with acceptable toxicity. First results indicate that perhaps more R0 resections may be possible compared to surgery alone.

496 POSTER

Serum levels of vascular endothelial growth factor (VEGF) and basic fibroblast growth factor (bFGF) in patients (pts) with soft tissue sarcoma (STS)

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Purpose: To determine if elevated circulating levels of VEGF and bFGF can be detected in sera from pts with STS.

Methods: 18 healthy controls and 55 STS pts were enrolled in this study. In STS pts sera were drawn prior to initial resection (IR) n = 31 or prior to wide reexcision (WR) 2–4 weeks after inadaequate local excision n = 24. VEGF and bFGF levels were determined by ELISA.

Results: Mean levels pg/ml (range) for VEGF and bFGF in healthy controls were 167 (22–404) and 3 (1–9). In STS pts with IR, VEGF levels were 628 (64–2000) and bFGF levels 16 (1–50). 17 STS pts with evidence of disease after WR showed following serum levels: VEGF 515 (44–2000), bFGF 26 (1–78). For 7 STS pts with no evidence of disease after WR the VEGF and bFGF levels were 350 (94–1150) and 23 (1–58).

Conclusion: Elevated VEGF and bFGF levels can be detected in sera from STS pts. Consecutive monitoring of VEGF and bFGF in the serum of STS pts might be a valuable new marker to monitor the tumor follow up.

497 POSTER

Intraoperative (IORT) and external beam radiotherapy (EBRT) for extremity sarcomas

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Purpose: IORT offers maximum sparing of mobile radiosensitive tissues. Organs and tissues of the extremities are less radiosensitive. Nevertheless the minimum effective dose for soft tissue sarcomas should be >66 Gy. Late complications and subsequent limb function are related to dose and irradiated tissue volume.

Patients and Methods: 25 patients (mean age 51.5 years), suffering from a stage IIB–IIIB extremity sarcoma had IORT between 7/91–5/95 (recurrent sarcomas n = 10). 4 pat. revealed microscopically residual disease after surgery. IORT dose was 15.3 Gy (15–20 Gy), using a field size 5–26 cm. Mean EBRT dose was 44 Gy.

Results: After a median follow-up of 28.8 months a 92% local control rate could be achieved. The local control rate was independent of the extent of surgical margins and tumor stage. 2 pat. had a lymph node failure, 5 pat. a distant failure. The actuarial overall and disease-free survival was 77% and 58% at 4 years. Perioperative morbidity occurred in 17% of pat., requiring additional surgical treatment in 11% of pat. In 14% of patients a late adverse effect was observed.

Conclusion: Combined surgical resection and IORT for locally advanced extremity sarcomas can provide excellent local control. In view of the reduced late morbidity with subsequent good limb function, the results are encouraging.

498 POSTER

Retroperitoneal sarcomas – Prognostic value of ploidy and other important factors

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Purpose: Grading and type of surgery are very important for prognosis in all types of sarcomas. For the better understanding of outcomes and possibilities of treatment retrospective analysis of different factors, including DNA content, was performed in retroperitoneal sarcomas.

Methods: The study was based on 70 patients treated between 1965 and 1994. Leiomyosarcoma and liposarcoma were most common histologic type of classified sarcomas. Different kinds of resection were performed in 49 patients and 33 of theirs available DNA specimens were analysed.

Results: The actuarial 5-years survival rate in resection group was 53% with the median survival of 57 months (compared with 10 months without resection). Patients with diploid resected tumours had better 5-years survival rate (58%), than with aneuploid (25%) – $P < 0.005$. Patients with grade I and II sarcomas had a significantly longer survival than with grade III (5-years survival rate 44% compared with 29%). There was no influence of adjuvant therapy, histology, type of surgery, localisation of tumour and S-phase on survival in the univariate analysis. In the multivariate analysis (Cox), only ploidy was independent prognostic variables for survival. Relative risk of death was over 3 times higher for aneuploid than for diploid tumours.

Conclusion: The DNA content analysis is an important prognostic factor, which should be performed in every case of retroperitoneal sarcoma for better follow-up and possibility of adjuvant therapy.

499 POSTER

Ifosfamide (IFO) in continuous infusion (C.I.) for 21 days as second line therapy in advanced sarcomas: A phase I study

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Ifosfamide is an alkylating agent active in advanced soft tissue and bone sarcomas. Generally we distinguish between conventional doses and high doses (from 10 to 15 g/sqm for cycle). High doses, delivered in 4–5 days, of c.i. must be reserved to good P.S. pts and request CSF support. In poor P.S. pts or as a second-line therapy, the same total dose can be administered in longer time in order to avoid heavy toxicities with a comparable relative dose intensity. From this rationale, we planned a 21 days-therapy using a low-daily-dose (1 g/sqm). The solution including Ifo and Mesna (1 g/sqm/day equidose), was administered by portable pump as outpatient therapy. Pump was changed every 3 days and the course should be completed at 21st day. Therapy was discontinued until recovery when neutrofil counts was <1500/mm^3 or creatinine >1.5 mg/dl. 6 patients (3 male, 3 female) with advanced soft tissue and bone sarcomas, relapsed after first line CT, entered the study. Mean P.S. was 1 and mean age was 37.5 years (median 35). 15 courses were administered (mean 2.5, median 3). No course was completed in 21 days. Only one was completed in 28 days and 14 in more than 28 days. Definitive D.I. was 63%. The delay was due to grade 3 but rapidly recovering mielotoxicity. No other side effects were seen. Generally toxicity appeared after 15 days of c.i. We recorded 1 CR (pelvis relapse of Ewing sarcoma), 1 PR and 4 PD.

Conclusions: Low doses of Ifo as a c.i. in advanced sarcomas seems to be a promising therapy with a good activity and a mild toxicity. However, 21 days c.i. is too much for pretreated patients; in a new protocol we'll use the same daily dose but only for 15 days infusion.

500 POSTER

Evidence of circulating tumor cells of Ewing's sarcoma is associated with higher incidence of local relapse and metastatic spread

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Background: Different variables have been studied to predict the probability of recurrence and metastases in patients diagnosed of Ewing"s sarcoma. In this study, we have evaluated the presence of tumor cells of Ewing"s sarcoma (ES) in peripheral blood samples through a reverse-transcriptase polymerase chain-reaction (RT-PCR).