The prognostic is generally fatal. Histologically, they are malignant histiocyto-fibrosarcomas in the majority of the cases.

In order to determine their risk and prognostic factors, we have decided to study all the post-radiation sarcomas diagnosed from 1975 to December 1994 in nine French anti-cancer centers.

116 cases have been included in this study. When possible, all the cases will be reviewed by the pathologists of the Sarcoma Group of the FNCLCC (Dr J. Simony-Lafontaine, Dr J.M. Coindre) to confirm the diagnosis and the histologic types. Our preliminary results will be presented and all the French anti-cancer centers are invited to participate in this study.

851 ORAL

CHORDOMA—A RARE AND LETHAL DISEASE

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In Denmark only 1–2 chordomas are diagnosed per year. In this national Danish study 37 patients with histological proven chordoma were analyzed. Male:female ratio was 2.7:1. Median age was 59 years (range 1–83). Median duration of symptoms before admission was 12 months (1–84). Dominating symptoms were pain (98%), neurological disturbances (42%) and incontinence (33%). The tumours were located in the sacro-coccygeal region in 68%, spheno-occipital region in 16% and vertebrae in 16% of the patients. Median tumour size was 7 cm (1–30). Treatment was surgical resection in 11, radiation in 10 and a combination of the two in 15 patients. Median radiation dose/fractions were 55 Gy (30–80)/29 (13–50). Symptom relief was obtained in 85% of the patients (67% complete), and the median time to maximum relief was 7 months (5–46). Two patients were lost for follow-up. At the time of analysis 10 patients were alive. Only 4 patients were without symptoms. Distant metastases developed in 23%. The actuarial 5-/10-year rates of overall, progression-free and symptom-free survival were 40%/26%, 31%/21%, and 20%/14%, respectively. Patients with active chordoma may live for a long period but often suffer from pain and other symptoms. The ultimate prognosis of chordomas is very poor.

852 POSTER

ADJUVANT RADIATION THERAPY FOR SOFT TISSUE SARCOMAS OF THE EXTREMITIES

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Between Jan 1990 and Dec 1994, 32 patients with soft tissue sarcomas of the extremities were treated; the mean age was 45 (10–81); 19 were female; 23 had Stage IIIB tumors. Group A consisted of 22 patients who underwent placement of afterloading catheters at the time of resection of their tumor. Patients received a mean dose of 22 Gy (10–30) at a dose rate of 10 Gy/day, with Ir-192. Subsequent external beam radiation therapy (RT) to give total doses of 55–70 Gy was delivered. Group B consisted of 10 patients who received postoperative external beam RT alone to doses of 45–70 Gy. With a mean follow-up of 23 mo (3–60), the overall local control is 78% (86% Group A and 60% Group B). Of the 7 patients who failed locally, 2 were salvaged with amputation and are without evidence of disease; 1 died of uncontrolled local disease and 4 died of distant metastases. Thirty percent of patients developed distant metastases. Adjuvant RT yields excellent local control in patients with large tumors of high grade. There appears to be a trend toward better local control in patients receiving brachytherapy.

853 POSTER

IFOSFAMIDE IN CONTINUOUS INFUSION: THE PHARMACOKINETIC PROFILE IN PATIENTS WITH SOFT TISSUE SARCOMAS

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On behalf of Italian Group of Uncommon Tumours

Ifosfamide, an oxazophosphorin compound, active in mesenchimal tumours has recently been used at high doses (14–18 g/sqm) in order to increase the number of responses. Continuous infusion (C.I.) of Ifosfamide probably decreases toxicity and increases the therapeutic window of the drug. Bone marrow and renal toxicities seem to be modified greatly by C.I.. Aim of our study has been to characterize the pharmacokinetic drug profile during C.I. high dose-fosfamide (HD-IFO). From April to December 1994, 9 patients (pts) with advanced soft tissue sarcomas, 5 pts with osteosarcomas and 1 pts with Ewing's sarcoma with normal liver and renal function, treated with C.I. HD-IFO (14 g/sqm. over 4 days) and Mesna contemporary infusion, entered into the study. 33 chemotherapy courses were administered (range 1–4, mean 2.2). Pts were submitted to blood sampling previous starting of infusion, and 12, 24, 48, 72, 96, 100, 104, 114, and 120 hours after treatment beginning. Plasma samples were stored at 0°C. Chemical analysis was performed using HPLC. Maximum concentration of the drug was observed at 24th hour (C_{24}: 61.5 ± 21.9 μg/mL.) while decreased pseudo-steady rate levels were reached after 70–80 hours (Css: 28.3 ± 11.5 μg/ml). Terminal half life was 3.2 ± 0.4 hours; AUC (following trapezoidal rule) was 3654 ± 1222 mg/l. × hour. Median Clearances (total dose / AUC) was 7.14 ± 3.3 l/h. At the second or following cycles a relevant reduction of T1/2 and AUC (−20% and −25%) due to enzymatic autoinduction was observed. In confront with Ifosfamide administration at the same doses but in 1 hour infusion we observed that C.I. leads to a higher AUC (3650 vs. 1230) to a shorter T1/2 (3.2 h. vs. 5.9 h.) and to a relevant increase of total clearance (7.14 vs. 3.9).

This significant difference in pharmacokinetic profile can explain the different spectrum of activity between the two manners of administration.

854 POSTER

LEIOMYOSARCOMAS (LMS), MALIGNANT MÜLLERIAN MIXED TUMORS (MMT) AND ENDOMETRIAL STROMASARCOMAS (ESS) OF THE UTERUS: DIFFERENCES IN TREATMENT AND PROGNOSIS?

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Objectives: Uterine sarcomas are very rare tumors with a poor prognosis. Present study was undertaken to examine the treatment strategies, the clinical outcome and the aftercare management problems on the background of different prognostic factors.

Material & Method: 75 LMS, 21 MMT, 35 ESS, 1 reticulosarcoma, and 6 no classificable sarcomas (NCS) treated between 1969 to 1994, were evaluated retrospectively. Treatment strategies consisted of surgery, surgery/radiation, surgery/radiation/chemotherapy.

Results: Overall 5-year survival probability was 62%, but it was different in LMS, ESS and MMT. 24% of LMS, 28.6% of MMT, 17.1% of ESS and 28.6% of NCS show No Change or developed local recurrences and/or metastasis. Patients died 6 months after recurrence. *Conclusions:* Adjuvant irradiation seems to be important in the management of uterine sarcomas.

855 POSTER

THE USE OF R-MET HU 6-CSF IN COMBINATION WITH HIGH AND STANDARD DOSES OF IFOSFAMIDE AND DOXORUBICIN IN THE PATIENTS WITH ADVANCED SOFT TISSUE SARCOMA

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Sixty patients with stage III-B and IV soft tissue sarcomas were randomised to receive either Ifosfamide: 5 g/m² × d × 1 and doxorubicin: 60 mg/m² × d × 1 given every 3 weeks or Ifosfamide: 1.8 g/m² × d × 5 and doxorubicin 60 mg/m² × d × 1 given every 4 weeks. The granulocyte colony stimulating factor (r-set Hu 6-CSF: 250 μg/m² × d) was applied with a prophylactic intent in the first group as it was given preemptively in the other group. The response rate was higher in the high dose Ifosfamide receiving group (56% versus 33%, $P = 0.03$). In stage III patients, the CR rate was significantly higher (53% versus, 13.3%, $P = 0.01$) and the duration of response was significantly longer in the high dose Ifosfamide receiving group (20 ± 8.2 months versus, 13.4 ± 7 months, $P = 0.05$). Chemotherapy related myelotoxicity and mucositis were also less frequent in the first group as a result of prophylactic r-met Hu 6-CSF administration ($P = 0.04$, $P = 0.003$).

It was concluded that high dose Ifosfamide and doxorubicin combinations deserve further investigation under the cover of hematopoietic growth factors particularly in patients with stage III soft tissue sarcomas.