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EFFICACY OF LENOGRASTIM ON HEMATOLOGICAL TOLERANCE TO MAID CHEMOTHERAPY IN SARCOMA PATIENTS AND IMPACT ON DOSE INTENSITY.

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From 8/90 to 10/91, 48 patients with an advanced soft tissue or visceral sarcoma to be treated with MAID were included in this study, to assess the effects of lenograstim on hematologic tolerance to treatment and on dose intensity of successive chemotherapy cycles. After the first MAID cycle (3 days), patients were randomised to receive 10 days of either lenograstim (G. group) or placebo (P. group) at 5 µg/kg/day by S.C. route, beginning on day 4. Results are summarised below.

	Neutro. <500/mm³ med. duration (range)	Neutro. <1000/mm³ med duration (range)	Neutro. count recovery >1000/mm³ med.time (range)	Pts with febrile neutropenia (mean duration)
P group (26 pts)	5 (0-10)	7 (4-14)	17 (14-21)	15 (3.5)
G group (22 pts)	0 (0-3)	2 (0-5)	12 (10-13)	5 (0-4)
p value	<0.001	<0.001	<0.001	0.002

Thirty-one patients were to continue with MAID at the same dose, with systematic lenograstim. Results are presented below.

	Cycle 2 (28 pts)	Cycle 3 (26 pts)	Cycle 4 (22 pts)	Cycle 5 (18 pts)	Cycle 6 (13 pts)
Relative dose intensity	0.954	0.951	0.959	0.978	0.756
Febrile neutropenia episodes	8	7	10	6	7
(mean duration)	(0.5)	(0.4)	(0.5)	(0.3)	(1.2)

At the present time 13/27 evaluable patients (38 %) present a tumor reduction ≥ 50 %. In conclusion, lenograstim significantly reduces neutropenia duration in patients receiving the markedly myelosuppressive MAID regimen and allows the continuation of chemotherapy at optimal dose intensity in most patients. Whether or not chemotherapy doses can be increased is a question addressed in another paper.

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DOSE INTENSIVE TREATMENT OF OSTEOGENIC SARCOMA. THE "BIG MAC" PILOT STUDY.

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A correlation between dose intensity & survival has been suggested by analysis of studies of breast cancer, lymphoma and osteogenic sarcoma.Starting 9/1987, a pilot study was performed to assess the effect of doubling the dose intensity of the then current methrotrexate cisplatinum adramycin protocol in compliant non-metastatic classical limb primary osteogenic sarcoma. 12 patients received elements of "BIG MAC" high dose methotrexate 12-20gm/m2 weekly x 2 weeks followed 1 week later by adriamycin 30 mg/m2 over 3 hours for 3 days and simultaneous cisplatinum 200 mg/m2 over 5 days. Definitive surgery was performed after 2 of 4 elements followed by 6 MTX treatments. VP16 100mg/m2x5 days and ifosphamide 1.8gm/m2 x5 days were given if cardiotoxocity or ototoxicity prevented adequate treatment or if tumor was found at surgery. 83% (10/12 patients) are alive and event-free (followup 2.25-5 yrs). This compares favorably with 64% (9/14)& 33%(3/9) achieved in the 2 previous protocols '80-87 and '73-79.

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PRIMARY BONE TUMOR RESECTABILITY: THE VALUE OF SERIAL MRI STUDIES IN THE DETERMINATION OF THE FEASIBILITY, TIMING AND EXTENT OF RESECTION

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A prospective analysis of 129 MRI studies in 50 patients with primary bone tumors, performed from January 1984 to December 1990, was conducted to evaluate the contribution of serial MRI studies in the determination of the feasibilty, timing and extent of tumor resection.Long TR-long TE T2 weighted (T2 2nd echo) imaging was the most useful in assessing soft tissue involvement, and short TR-short TE T1 weighted (T1) imaging, for documenting bone marrow changes. Twenty successful resections were performed with only one local recurrence. One study falsely suggested active tumor. In 4 other cases the MRI was useful. Nineteen patients with nonmetastatic disease had resections based on MRI; of these 18 (95%) are alive and well, 15(79%) are event-free (follow-up of survivors is between 2.5-8 years).

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FLOW CYTOMETRY DNA PLOIDY ANALYSIS IN CHILDREN WITH RHABDOMYOSARCOMA AND SOFT TISSUE SARCOMA

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Flow cytometric DNA analysis was performed in 58 children with Rhabdomyosarcoma and soft tissue sarcoma. The study was performed retrospectively on deparaffinized tissue blocks and results were correlated with known prognostic factors. DNA index (DI) of 1-1.2, 1.2-1.7, and over 1.7 was considered as Diploid, Hyperdiploid and Tetraploid, respectively. In cases where few clones were found, the DI of the main population was considered. 35 (60%) children presented with embryonal rhabdomyosarcoma, 10 (18%) with alveolar subtype and 13 (22%) with soft tissue sarcoma. DI Diploid, Hyperdiploid and Tetraploid was found in 24%, 43% and 33% of the patients respectively. In 10 children - multiclonal disease with various DI. was observed. Life table and univariate analysis, by histology, primary site, tumor size, clinical staging and relapse - could not demonstrate any significant correlation with DI. It is suggested, that the successful current therapy in childhood rhabdomyosarcoma may have abrogated the prognostic contribution of DNA content.

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RADIOTHERAPY (RT) AND RAZOXANE IN THE TREATMENT OF SOFT TISSUE SARCOMAS: FINAL RESULTS OF A RANDOMIZED STUDY (1978-1988)

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MATERIALS & METHODS: Between 1978 and 1988 144 patients have entered the study, 128 were evaluable. Median dose of radiation: 60 Gy in both groups. Razoxane was given by mouth at a daily dose of 150 mg/M2 during the time of the radiotherapy starting 5 days before the first irrad. The groups were comparable as to their prognostic factors.

RESULTS: In 82 patients with inoperable, residual or metastatic disease the combined treatment produced higher CR and PR rates compared to photon irradiation alone (74 vs 49%). The local control was 64% in the razoxane-group and 31% with photon irradiation alone ($p < 0.005$). Among 46 patients treated postoperativly without residual disease there were no significant differences in local control and survival between the two groups. The acute toxicity was slightly higher in the sensitizer-arms, no difference was seen in late complications.
CONCLUSION: RT and Razox. improves the local control in inoperable, resid. or recurr. STS compared to RT alone.

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ADRIAMYCIN (ADR) IN HYPERTHERMIC ANTIBLASTIC PERFUSION (HAP) FOR HIGH GRADE (HG) LIMB SARCOMAS.

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In 25 patients with limb sarcoma ADR was administered via HAP prior to surgery. Tumor necrosis was then ascertained in order to evaluate the activity of ADR under these conditions. Two patients were AJC stage 2a, 4 stage 2b, 1 stage 3a, 12 stage 3b and 6 stage 4b. ADR (bolus, 0.7 - 1.4 mg/kg) was given at 40.5°C tumor temperature (range 40.5 - 42.6°C) and perfused for 60 mins. Systemic toxicity was hematologic grade (G) I in 3 patients, gastrointestinal GI in 2, GII in 3 and GIII in 1; locoregional toxicity was GI or GII in 18, GII in 4 and GIV in 1 . Tumor necrosis (radiological and histological evaluations) was > 50% in 18 patients (72%). Limb-sparing surgery was feasible in 22 patients (91.6%). At present 16 patients are alive. Six had local recurrences and 8 distant metastases. HAP with ADR seems to be an active and well tolerated procedure within a multidisciplinary approach to limb sarcomas.