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INTENSIFIED ADJUVANT CHEMOTHERAPY FOR EXTREMITY SOFT TISSUE SARCOMAS (STS)

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Adjuvant chemotherapy for STS still remains a matter of debate, since just few randomized studies have indicated a small advantage in terms of disease free interval or overall survival at preliminary reports. However, the majority of those trials have not included adequate doses of anthracyclines nor the today most active agent Ifosfamide (IFO). To re-evaluate the role of adjuvant chemotherapy in extremity STS, we started in June '92, a co-operative randomized prospective adjuvant study comparing a control arm to an intensified chemotherapy arm. Treatment consisted of Epirubicin 60 mg/m^2, day 1&2, Ifosfamide 1.8 g/m^2 × 5days as 1 hr infusion, MESNA 60% of the daily IFO dose fractionated in 3 separated doses, fluids 1.5–2.0 litres/day and G-CSF 300 μg/day from +8 to +15; treatment was scheduled every 3 weeks for a total of 5 cycles. Of the 37 up to now randomized pts to the chemotherapy arm, 25 are evaluable (5 cycles completed + two months follow-up) for the toxicity and dose intensity evaluation purpose (12 pts not yet evaluable). The median nadir of WBC and PLTS was 1300/μl (range: 200–8000/μl) and, 120000/μl (range: 10000–250000/μl), respectively. Overall, a G4 leukopenia and thrombocytopenia was noted in 30% and 5% of cycles respectively. Anemia progressively worsened and the median Hb fall from basal values to the nadir of the 5th cycle was of 4 g/dl (range: 0–9.8 g/dl); in 12 of 25 pts (48%) PRBC transfusions were given to prevent symptoms from anemia. Nevertheless, an optimal recovery to pre-treatment values was obtained after 2 months from end of treatment (median Hb 13.5; range: 12.7–14.8). Neutropenic fever was observed in 15% of the cycles, prophylactic antibiotics were administered in further 3% of cycles. No pts received plts support. The median average received dose intensity (ARDI) was of 91% (range: 67–100%) and 19/25 pts (76%) received an ARDI > 80%. Causes of reduction in dose intensity were delay in retreatment in 24 cycles and reduction of the dose in 40 cycles. Even through the toxicity was substantial (anemia and leukopenia) it was possible to give an adequate dose intensity to the majority of pts. All but one pt (3 cycles received) completed the forseen 5 cycles employing the predefined dose reduction schema.

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INCREASING CONTINUOUS INFUSION (C.I.) IFOSFAMIDE (IFO) AND BOLUS EPIRUBICIN (EPI) IN SOFT TISSUE SARCOMA (STS) PATIENTS (PTS)

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There is a direct relationship between the dose of IFO and EPI and the clinical response achievable in STS. We have, therefore, associated full doses of EPI (60 mg/m^2 × 2 d, 1 hr inf.) to increasing c.i. IFO + MESNA and G-CSF (300 μg/d, +7 to +14) in order to evaluate the maximum tolerated dose (MTD) of this program and obtain information on the clinical activity. The IFO starting dose level was 9 g/m^2 (72 hrs c.i.); further planned levels are 10.5 g/m^2 (84 hrs) and 12 g/m^2 (96 hrs). Eval for the definition of the MTD are those pts completing 3 consecutive cycles or developing a DLT. A DLT corresponded to: a G4 leucopenia or thrombocytopenia ≥ 5 day; any G3 neuro-nefrotoxicity; any other G4 toxicity. In case of 1 dose limiting toxicity (DLT) observed in the first 10 evaluable (eval) pts, the level is considered safe and closed; in case of 2 DLT the accrual of pts is pursued up to 15 eval pts. The MTD is defined as the level in which 3 pts/15 eval develop a DLT (20%). Since 09/93, 28 pts with advanced previously untreated STS have been entered in the first 2 levels. Patients characteristics are: 14 males, 14 females, median age 49 (19–66), median PS (0–2); site of origin was extraskeletal in 20, visceral in 8. Measurable/evaluable parameters were present in 25 pts. Overall, 13 pts entered the first level: 1 early PRO, 2 not eval and 10 eval for the MTD definition (1DLT); 15 entered the second level: 2 early PRO, 2 not oval, 4 in progress and 7 eval for the MTD definition (2DLT). The study is ongoing in order to complete the second level (15 eval pts).

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DIAGNOSIS, TREATMENT, RESULTS AND FOLLOW-UP OF SARCOMAS OF THE JAWS

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We have examined 149 patients with sarcomas of the jaws: 86 cases with upper jaw tumors and 63 cases with low one. The most common tumors were osteogenic sarcoma. (22.1%), chondrosarcoma (21.5%) and malignant fibrous histiocytoma (9.4%). All patients underwent X-ray examination and 38-computed tomography. The diagnosis was verified by FNA cytology (76 patients) and biopsy (122 patients). The main method of treatment was surgical or combination therapy, that were performed at 117 patients. 5-years survival rate was 49%. 11 patients with radiosensitive tumors were treated by radiation and chemotherapy with 50%. 5-years survival rate. Recurrences were determined in 54 patients (49%). Surgical treatment is a method of choice of recurrence of jaw's sarcoma with 49% 5-years survival rate. Multi-component cellular composition and wide range of tumors histological variants as well as the fact that they are situated in sophisticated anatomic topographic region demand great attention and professional training of all specialists.

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CELL MEMBRANE SIALOGLYCOLIPIDS AND DISSEMINATION IN BONE TUMOURS

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Level and profile of gangliosides were studied in osteogenic and chondrosarcoma cells. Level of lipid-binding sialic acids in bone- and cartilage-producing tumours proved different. Most osteogenic sarcoma samples showed higher level of lipid-binding sialic acids as compared to chondrosarcoma. In the latter tumor, level of lipid-binding sialic acids was related to grade of tumor cell differentiation, peak levels being observed in undifferentiated neoplasma as compared to those showing grade I–II cell anaplasia. Chondro- and osteogenic sarcoma revealed different profiles of sialoglycolipids, particularly, due to markedly reduced set of gangliosides and nearly complete loss of polysialogangliosides in the latter tumor.

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A CLINICAL AND PATHOLOGICAL STUDY OF MALIGNANT NON-EPITHELIAL AND MIXED TUMOURS OF THE UTERUS

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We reviewed retrospectively 94 cases of malignancies non-epithelial tumours of the uterus collected at Cancer Research Center in Moscow. Median age of the women was 49 years and 44.5% had postmenopausal status at the time of the initial diagnosis.

High per cent of diagnostic mistakes are attributed by the difficulties in pathology of the malignancies non-epithelial tumours of the uterus.

Most important diagnostic and prognostic criteria for uterine sarcomas are the following: size of the tumour, mitotic activity and histological patterns.

Combined treatment is considered most adequate for sarcomas of the uterus. Radical surgery has to be followed by adjuvant chemotherapy as well as post-operative radiotherapy in some cases can be recommended.

5-year overall survival in our series of patients with sarcoma of the uteri constitutes 34.1%. According to histotype of the tumour we observed 39.4% in leiomyosarcomas, 68.6% in endometrial stromal sarcomas and 7.7% in mixed mesodermal tumors respectively within 5-years of follow up. Our analysis revealed that haematogenous dissemination is the commonest for sarcoma of the uteri and was seen in 57.5% of the cases as the first sign of relapse.

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TREATMENT OF ADVANCED SOFT TISSUE SARCOMAS (STS) WITH HIGH DOSE EPIRUBICIN (HD-EPI)

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The evidence of a dose-response effect to anthracyclines in advanced STS prompted us to begin a clinical trial with HD-EPI. We have already reported (Proc ASCO 11:414, 1992) a 14% response rate with EPI 120 mg/m^2 iv q 3 weeks in 36 sarcoma pts. Since April 1991, 48 pts were treated with EPI 160 mg/m^2 iv q 3 weeks. Clinical characteristics of pts are the following: M/F = 26/22, median age = 52 years