1071 POSTER DISCUSSION

The aggressiveness of hypoxic soft tissue sarcomas cannot be explained by mutations in the TP53 gene

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Purpose: Tumor hypoxia and TP53 mutations are two parameters suggested to have a negative impact on survival probability in human tumors. Also, In-vitro studies have shown that hypoxia induce apoptosis in p53 −/− cells tumor cells. The present study was performed to evaluate the relationship between TP53 mutations and tumor hypoxia in human soft tissue sarcomas (STS).

Methods: Pretreatment tumor oxygenation was measured using polarographic oxygen electrodes (Eppendorf, Germany) in 26 conscious patients with primary STS. Oxygenation parameters was tumor median pO2 and the percentage of pO2 values 2.5 mmHg (HF2.5). Gene mutations (in exons 2–11) were studied in material deriving from either fresh frozen tumor biopsies or paraffin-embedded tissue sections and using Denaturing Gradient Gel Electrophoresis (DGGE) as the initial scanning procedure and characterized by sequencing.

Results: TP53 mutations were identified in 6 tumors. The oxygenation status of these 6 tumors was high as the grand median of the tumor median pO2 was 24 mmHg (range 14–32) and a median HF2.5 of 2% (range 0–6). Five tumors with TP53 mutations were histopathologically grade IIIa–IIIb and the last grade III not otherwise specified.

Conclusion: These preliminary results show that in soft tissue sarcomas the aggressiveness of hypoxic tumors was not explained by TP53 mutations.

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The comparison of 2 protocols for treatment of osteosarcoma (OS) with or without escalation of HDMTX enhances the high value of MTX individual adaptation

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Purpose: To demonstrate the role of HDMX adaptation in long term survival of patients (p.) with high grade OS, we compared our results in 2 successive OS protocols.

Methods: From 85 to 95, 90 p. with primary high grade OS fulfilled the classical criteria: non metastatic, resectable tumor, previously untreated. **Group 1** (G1): 45 p. received a fixed dose of MTX adapted only to age. **Group 2** (G2): 45 p. received escalating doses of MTX with PK and clinical monitoring.

Results: In G2, a dose escalation was necessary in nearly 70% of cases (32/45) due to low serum concentration (15), or lack of clinical response (9) or both (8). G1 p. received a mean dose of 10.5 g/m^2/course and G2 p. a mean dose of 13.5 g/m^2/course (mean seric concentration of respectively 850 μmol/l and 1175 μmol/l). No significant difference in toxicity was observed **Outcome** the overall survival and DFS at 5 (and 10) y. are respectively **71% (69%) for G1** (fixed dose of MTX), **93% (91%) for G2. The differences are statistically significant.**

Conclusion: The serum peak and AUC are correlated with the rate of GR. The seric intensity is correlated with the late DFS. Individual PK of MTX, supplemented by careful examination of the tumoral limb before each course of MTX led to increase the dose of MTX in 70% of p., resulting in more GR and more late survivors without significant increase of toxicity.

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Advanced soft tissue sarcoma (ASTS): Neoadjuvant chemotherapy may allow more conservative surgery

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Purpose: The II trial. Evaluation of functionnal improvement of surgery and outcome.

Medhod: 48 patients have been included in this ongoing study since April 1996. Median age 44 years. 33 pts had a locally ASTS and 15 had metastasis, primary tumors were located to the trunc and limbs. An intensive neoadjuvant regimen (API-AI) consisting in two cycles (4 courses) of chemotherapy was designed. Doxorubicine 60 mg/m^2 (D1, D15), Cisplatinum 100 mg/m^2 (D1), Ifosfamide 5 g/m^2 (D2, D15) with an equivalent dose of mesna. G-CSF was added after each course for 6 days (D6–11 and D19–24).

Results: 44 patients are evaluable for response.

Table 1:

Clinical Response	Locally ASTS (29)	Metastasis (15)
C.R.	0	1
P.R.	10	7
O.R.	10 (35%)	8 (53%)
S.D.	16 (55%)	4 (27%)
P.D.	3 (10%)	3 (20%)

Among the 29 operated patients, 10 (35%) had more conservative surgery and avoided abdomino perineal or limb amputations.

Conclusion: Neoadjuvant chemotherapy allows to modify surgery in a more conservative way in 35% of ASTS. It seems very interesting if mutilating surgery is considered at first. There is no parralelism between clinical and histological response. Survival impact must be evaluated by further study.

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Retroperitoneal soft tissue sarcoma: A difficult diagnosis

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Purpose: Succesfull surgery of retroperitoneal soft tissue sarcoma (RSTS) is dependent on preoperative planning, only possible when the diagnosis is established before definitive treatment. In a population based study, the share of patients was determined in whom the diagnosis was established only after definitive treatment. Factors contributing to an erroneous diagnosis were analysed and the influence on outcome of treatment evaluated.

Method: In a nation-wide study eligible data were collected on 126 patients with RSTS between 1989–1993. Mean age was 56 yrs., M/F ratio was 57/69. Patients were categorised as diagnosed correctly (group 1) or erroneously (group 2) before definitive treatment.

Results: Forty percent of all patients (51/126) were initially treated for assumed other disease. The clinical presentation was similar in both groups, although 8 of 10 patients with an acute presentation were in group 2. Tumour histology, malignancy grade and localisation were the same. The tumours of patients in group 2 were smaller (median diameter 12 cm. vs. 20 cm.; $p < 0.05$). Clinical work-up in group 2 contained less frequently CT-imaging (62% vs. 89%; $p < 0.001$) and biopsy (64% vs. 20%; $p < 0.001$). Treatment of the 75 patients in group 1 led to abandonment of surgical treatment in 12 and complete resection in 47 of the 63 remaining patients (75%). Surgery in 49 patients in group 2 resulted in complete resection in 27 patients (55%).

Conclusion: Forty percent of patients with RSTS were treated for assumed other diagnoses. Incomplete work-up was a contributory factor in a minority of these patients. Despite smaller tumours, treatment of preoperative erroneously diagnosed patients resulted in less complete resections.

1075 POSTER

Significant improvement of relapse free survival as well as time to distant failure for adult grade 3 soft tissue sarcoma after adjuvant augmented chemotherapy plus adjuvant hyperfractionated accelerated radiotherapy: A prospective randomized trial of the Austrian cooperative soft tissue sarcoma study group

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The present prospective randomized trial was carried out to compare the efficacy and toxicity of adjuvant augmented chemotherapy (ACT) added to adjuvant hyperfractionated accelerated radiotherapy (HA-RT) after wide or marginal resection of soft tissue sarcoma (STS). 59 patients underwent primary surgery by wide or marginal excision and were subsequently randomized to receive either adjuvant HA-RT alone or under the addition of six courses of an adjuvant ACT containing ifosfamide (1500 mg/m^2, days