Discussion: It is believed that post chemotherapy new expression or no down-regulation of the erbB-4 molecule represents tumor aggressiveness and increased capability of growth and spread.

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Isolated limb infusion for the treatment of advanced extremity soft tissue sarcomas

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Extremity soft tissue sarcomas (STS) are often large at presentation and as a result resection without compromise to limb function can be difficult or impossible. Regional high dose chemotherapy can be used to avoid amputations in patients with advanced or recurrent STS. Isolated limb infusion (ILI) is such a technique, performed using percutaneous catheters, which makes it a simpler and less invasive procedure than conventional isolated limb perfusion (ILP). Response rates in patients with advanced melanoma after ILI with melphalan and actinomycin-D have been comparable with results obtained after ILP. To evaluate the role of ILI in advanced soft tissue sarcoma all patients treated with this technique at the Sydney Cancer Centre were studied to assess short and long- term results.

Between 1994-2000 a total of 19 patients underwent 20 ILI procedures (4 upper limbs, 15 lower limbs). Three patients presented with multiple tumours whereas all other patients had a single tumour. In all but one patient melphalan was used in combination with actinomycin-D (n=15), mitomycin-C (n=3) or both (n=1). The remaining patient was infused with a combination of mitomycin-C, adriamycin and cisplatin. In 9 patients the ILI was performed with the aim of decreasing tumour size and enabling a radical tumour resection. In the other 10 patients the ILI was performed for local control to avoid amputation and was not followed by surgical resection. All ILIs were performed under hypoxic and mild hyperthermic conditions (mean maximum temperature 37.8°C).

Wieberdink Grade II limb toxicity occurred in 7 patients, Grade III toxicity in 10 patients, and Grade IV toxicity in 3 patients. Fasciotomy was necessary in two of the latter group of patients. Overall clinical response after ILI was 79% (complete response 26%, partial response 53%, no change 11%, progressive disease 11%). None of the patients treated with an additional surgical resection of the tumour developed a local recurrence (mean follow-up 20 months (9-42)). Of the patients treated with ILI only, local control was maintained for a mean of 11 months (1-37). Four of these patients eventually came to amputation, and in one patient local control for a further period was achieved with local radiotherapy.

In conclusion, ILI for advanced STS using melphalan and actinomycin-D as the infused drugs is a feasible and useful technique, with low morbidity and a high overall clinical response rate.

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Histamine enhanced antitumor effect of docetaxel and dacarbazine in human clear cell sarcoma xenografts in nude mice

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Background: Clear cell sarcoma has melanocytic features and is intimately associated with tendons and aponeuroses. It is rare. In the Scandinavian sarcoma registry 18 cases (0,8%) of clear cell sarcoma were registered between 1986 and 1996. Extensive surgery so far the primary treatment.

The aim of the present study was to investigate if histamine enhances the antitumor effect of dacarbazine (DTIC) and docetaxel.

Method: Human clear cell sarcoma tumor tissue was obtained during operation of a 58-year old woman. The tumor (UMCCS-I) was maintained by serial s.c. transplantations in nude mice. DTIC (200mg/kg, i.p.) given 3 times with an interval of 2 days, docetaxel (20 mg/kg, i.p.) single dose and histamine (4 mg/kg, s.c.) daily, 5days per week was administered in tumorbearing nude mice. DTIC and docetaxel was given separately or in combination with histamine. Tumor volume in the groups (n=7) was measured repeatedly and compared with a control group (given saline i.p.). The antitumor effect is considered significant when TC-ratio is 0.4 or less.

Results: The tumors were followed until day 21. The lowest TC-ratio was noted at day 21 in the DTIC group - 0.54. The corresponding TC-ratio value for the combination histamine-DTIC was 0.37. In the docetaxel-group the lowest TC-ratio- 0.39 was observed at day 13. TC-ratio in the combination docetaxel-histamine was 0.33. The TC-ratio was reduced at all measuring occasions when histamine was given in adjunction with DTIC and docetaxel.

Conclusions: Histamine seems to enhance the antitumor effect of dacarbazine and docetaxel in this clear cell sarcoma tumor model.

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Primary soft tissue sarcomas of the extremities: Treatment outcome with postoperative radiotherapy

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Purpose: The outcome of adult patients with primary localized soft tissue sarcoma of the extremities with conservative surgery and adjuvant irradiation (RT) was evaluated.

Methods and Materials: From 1975 to 1996, 107 patients (pts) with a median age of 44 years (range, 16 to 86 years) were treated at the Institut Gustave Roussy (IGR) with conservative surgery and adjuvant radiotherapy. The median tumor size was 7 cm (range, 1 to 20 cm) with 27, 36 and 36% stage I, II and III respectively. Histologic examination revealed negative histologic margin in 16%, close or positive margin in 75.5%, grossely positive in 2% and undocumented in 6.5%. The most common histological subtype was: malignant fibrous histiocytoma (27%), synovialosarcoma (27%), liposarcoma (6.5%), and leiomyosarcoma (6.5%). The histologic grade was 1 for 14 patients (13%), 2 for 40 pts (37%), 3 for 50 pts (46%) and unknown for 3 pts (3%). All patients underwent a function-sparing surgery. Forty six patients (43%) were reoperated;residual tumor were found in 82% of pts (38/46). All adjuvant radiation therapy was performed at the IGR. The median external beam dose was 50 Gy (36-65). Chemotherapy was used selectively in 18 patients.

Results: With a median follow-up was 132 months (36-288), the 5- and 10-year local control rates were 81% [CI, 72-88%] and 74% [CI, 63-83%] respectively. The 5-year disease-free and overall survival rates were respectively 53% [CI, 43-62] and 69% [CI, 59-78]. Histologic grade was a significant predictor for local recurrence (p=0.04). There was no significant association between local recurrence and margin status, histology, re-resection, residual disease, size, RTdose, or depth. Significant independent adverse prognostic factors for DFS were RT dose less than 50 GY (p=0.008) and grade 3 tumors (p=0.02). Despite the moderate dose, a substantial rate of long-term side effects was observed. Most of these complications were mild or moderate. No patient had to be amputated because of treatment-related toxicity.

Conclusion: Based on our experience and a review of the literature, we concluded that, in the postoperative setting a radiation dose below 50 Gy did not seem optimal. The optimal dose and long-term sequelae should be evaluated in a prospective randomized trial.

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Localized osteosarcoma of adult patients: Comparison with pediatric population in the same institution over a 16-year period

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Objective: To evaluate outcome of patients (pts) with localized osteosarcoma (LO) treated in two Departments (Adult-AD- and Pediatric-PD) of IGR.

Methods: All pts treated for a LO with induction chemotherapy (CT) either in AD (n = 71) or in PD (n = 149) between 1982 and 1998 are included in the analysis. Pts treated in PD received a MTX-based regimen while 3 different protocols were used in AD: modified-T10 (1983–1992), DOX-CDDP (AP) (1983–1993) and DOX-CDDP-IFO (API-AI) since 1992 (ASCO-2001).

Results: Median age and median tumor size were 20.8 yr [15.4–63] and 10 cm [3–25] in AD and 12.4 yr [range = 4.4–20] and 12 cm [1–29] in PD respectively. High-dose MTX was more toxic in adults than in younger pts. Good responders to CT (≥95% necrosis) were 36% and 48% in AD and PD respectively (p = 0.08). In AD, this rate varied according to the protocol from 25% (AP), 30% (T10) to 48% (API-AI). The 5-year overall survival (OS) of the entire population was 73% [66–79%] and the event-free survival (EFS) was 60% [53–67%]. OS and EFS were significantly better in PD than in AD: 5-yr OS = 79% [72–85%] in PD versus 59% [46–70%] in AD (p = 0.001) and 5-yr EFS = 65% [57–73%] in PD versus 48% [36–61%] in AD (p = 0.003). This difference was similar when we restricted analysis to the teenagers (35 in AD and 33 pts in PD). The pts treated in AD with API-AI regimen had a similar EFS to those treated in PD.

Conclusion: Over this period of 16 years, pts treated in PD had a better outcome than pts treated in AD. However this difference seems to disappear