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Intralesional beta-interferon in combination with radiotherapy in advanced soft tissue sarcoma

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Objective: Primarily inoperable or marginally operable soft tissue sarcoma show a poor prognosis, 5-year survival 30% with definitive radiotherapy and/or chemotherapy. Interferon-β (IFN-β) demonstrated to be radiosensitizing in soft issue sarcoma. Our own in-vitro data and the following results of a phase-2 study led to a multi-center study with intralesional IFN-β and radiotherapy in soft tissue sarcoma.

Materials and Methods: 16 patients with recurrent, pretreated and histologically confirmed soft-tissue sarcoma were included. Pretreatment: surgery 16/16, chemotherapy 13/16, radiotherapy 12/16 (median 60 Gy, range 40–90); age 42 (19–72), male/female 7/9. All patients received a combination of 5×10^6 IU IFN-β intralesional 3×/week and radiotherapy 32 Gy (26–64), 1.8 Gy 5×/week Duration of combined treatment: median 8 weeks (6–10).

Results: 14/16 patients responded to therapy, 3/16 CR (12+, 36+, 60+ month), 8/16 PR (median 12 month+, 2–36+), 3/16 SD (4, 8, 15 month), 2/16 PD progression-free intervall median 12 months + (10–36 mo). 2 patients were successfully reoperated (1 RO, 1 R1) with function keeping surgery. No serious toxicities were observed.

Conclusion: The combination of intralesional IFN-β and radiotherapy represents an interesting treatment for patients with locally advanced or recurrent soft tissue sarcomas, especially in whom limb-sparing surgery cannot be performed. These results should be further evaluated and confirmed to integrate this treatment option in a first-line treatment concept

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Multicentric randomized trials for high grade osteogenic osteosarcoma (OS). Cost-effectiveness?

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Purpose: These last 20 y. chemotherapy (CT) of patients (p.) with OS has been dramatically improved. Nevertheless dilemmas and controversies have continuously developed.

Methods: This study of the last 20 y. tries to evaluate the benefice of randomized trials in term of DFS for p. and cost effectiveness for the community.

Results: The literature demonstrates the following facts: 1) the multicentric trials to verify the effectiveness of CT in OS delayed the systematic use of CT for 3 or 4 y. 2) Preliminary results of COSS 77–82 which falsely concluded that amputed p. had more chances of DFS than others, delayed the conservative surgery for 5 y.. The definitive conclusions of these trials invalidated their preliminary reports. 3) the superiority of Rosen's protocols leas been continuously challenged for 15 y., by randomized studies. But these trials didn't respect the most important backgrounds of Rosen's protocol (delay between 2 courses of MTX, individualization of MTX dose upon evaluation of clinical efficacy, too large hydration of p. receiving MTX, too long preoperative phase, too low numbers of MTX courses, etc.). Furthermore, independent evaluation of T7 and T10 demonstrates, 15 y. later, that these protocols remain the most effective in OS DFS at 10 y. and the fundamental value of HDMTX became evident by macro-analysis of all published trials on this subject (Cancer, 08/1996).

Conclusion: In OS, multicentric trials led always to worse results than pilot studies performed in big centers. They served only to convince reticent medical community of the necessity of CT in OS. In the same time, many p. let their limb or/and their life because of these bad trials.

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Osteosarcoma in childhood – Improved survival with reduced toxicity

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Purpose: The outcome and toxicity of a neoadjuvant chemotherapy regimen for the treatment of childhood osteosarcoma with the aim of maintaining survival but reducing long-term toxicity is described.

Methods: Between 1988 and 1996, informed consent was obtained from 21 patients for treatment with the Bristol Resistant Tumour Protocol (BRTP), four with metastases at presentation. Chemotherapy comprised ten, three-weekly courses of CEEV (carboplatin 500 mg/sq m on day 1, epirubicin 50 mg/sq m days 1 and 2, etoposide 150 mg/sq m days 1 and 2; vincristine 2 mg/sq m (max 2 mg) day 1) alternating with IVA (ifosfamide 2.5 G/sq m days 1 to 3, actinomycin 0.9 mg/sq m days 1 and 2; vincristine as in CEEV). High-dose methotrexate (8 to 12 G/sq m) could be added after surgery (scheduled to follow the third course of chemotherapy) for poor histological response. Organ toxicity was assessed by regular echocardiography and chromium 51 EDTA determination of glomerular filtration rate (GFR).

Results: With median follow-up of 66 months, actuarial 5-year survival for non-metastatic osteosarcoma is 82% with progression free survival being 70%. Including the 4 metastatic patients, there have been only 4 deaths with 3 other progresssions, now disease free for 95, 31 and 16 months. Chemotherapy was well tolerated. 103/105 (98%) courses of CEEV and 101/105 (96%) courses of IVA were administered as planned. Severe but manageable haematological toxicity (WHO grade 3 or 4) was common. No clinical cardiac toxicity was observed although one patient had a reduction in echocardiographic fractional shortening and ejection fraction measurements. The last 2 doses of epirubicin were omitted and subsequent echocardiography has returned to normal. Four of twenty-one patients (19%) required long-term electrolyte supplementation but this was not related to changes in GFR in all of them.

Conclusion: The BRTP is well tolerated and has resulted in excellent long-term survival for non-metastatic osteosarcoma in childhood. Long-term organ toxicity is confined to the kidney and is manifested as electrolyte loss. In all cases this has been easily controlled with oral supplements. Since these results are at least as good as those reported using more toxic regimens, a randomised comparison should be seriously considered.

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Proton radiation therapy for skull base chordomas and chondrosarcomas

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Objective: Local control, survival, and failure outcomes of 58 patients treated with fractionatel proton radiation therapy (PRT) were analyzed for treatment efficacy.

Methods: Between March 1992 and January 1998, 33 evaluable patients were treated for chordoma; 25, for chondrosarcoma. Following various surgical procedures, gross residual tumor was detected in 91%; 59% demonstrated brainstem involvement. Target doses ranged between 64.8 and 79.2 (mean: 70.7) Cobalt Gray Equivalent. Patients were followed from 7 to 75 (mean: 33) months.

Results: Ten patients (17%) failed locally, resulting in local control rates of 92% (23/25 patients) for chondrosarcomas and 76% (25/30 patients) for chordomas. Tumor volume and brainstem involvement influenced control. All tumors $\leq$ 25 ml remained locally controlled, compared to 56% of tumors >25 ml ($p = 0.02$); 94% of patients without brainstem involvement remained without recurrence versus 53% with involvement ($p = 0.04$). Three patients died of disease; one, of intercurrent disease. Actuarial 5-year survival rates were 100% (chondrosarcoma) and 79% (chordoma), respectively. Grade 3 and 4 late toxicities were observed in 4 patients (7%) and were symptomatic in 3 (5%).

Conclusion: High-dose PRT offers an excellent chance for durable tumor control and survival, with acceptable risks. All small- and medium-size tumors without demonstrable brainstem involvement have been controlled. Even patients with large tumors and disease abutting critical normal structures benefited.

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Functional results and complications after ablative and limb-saving therapy in lower extremity sarcoma of bone

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Purpose: The functional results and the complication rates after several limb-saving and ablative treatments because of lower extremity musculoskeletal sarcoma of bone were evaluated.

Methods: Seventy-seven surviving patients were evaluated according to the ISOLS functional rating system. Fifty-two patients had limb-saving and