1016

PROGNOSTIC SIGNIFICANCE OF DNA-CONTENT IN HUMAN SOFT TISSUE SARCOMAS

Budach, W.; Socha, B.; Budach, V.; Streffer*, C.; Sack, H:
Dept. of Radiation Oncology, * Dept. of Radiation Biology, Essen University, Hufelandstr. 55, 43 Essen 1, Germany.

The prognostic relevance of cellular DNA- content has been shown for a variety of human malignancies, however, only a few data concerning soft tissue sarcomas (STS) have been published. Biopsies of 81 patients with STS referred for primary or secondary surgery were analyzed by flow cytometry to determine cellular DNA- content of tumors. Most patients (54/81) had already one or more local recurrences at the time of first presentation at Essen University. The median age of the patients was 45 (14 to 79) years. Forty-four (54%) patients had euploid and 37 (46%) had aneuploid tumors. Age, sex, and tumor localization (trunk vs. extremity) were equally distributed between euploid and aneuploid sarcoma patients. The median follow up was 69 (9 - 312) months. The median survival time for patients with euploid STS was 56 months and for patients with aneuploid STS 26 months ($p<0.0001$). DNA- content was the most important independent prognostic factor in a multivariate analysis for overall survival ($p<0.001$) and likelihood of distant metastases ($p<0.01$), whereas local tumor control did not depend DNA- content. Grading, tumor site, and tumor size were of borderline significance. Histology, sex, and age were not found to be of prognostic significance for overall and disease free survival.

1017

ISOLATED LIMB PERFUSION (ILP) WITH HIGH DOSE TNF-α, GAMMA-IFN AND MELPHALAN IN PATIENTS WITH IRRESECTABLE SOFT TISSUE SARCOMAS: A HIGHLY EFFECTIVE LIMB SAVING PROCEDURE.

Schraffordt Koops .H, Eggermont AMM, Lienard D, Hoekstra HJ, Geel B van, Lejeune FJ. Departments of Surgical Oncology, University Hospital Groningen, Rotterdam Cancer Center, The Netherlands and CPO/CHUV, Lausanne, Switzerland.

Goal: To achieve limb salvage in patients with irresectable soft tissue sarcomas.
Methods: Twenty-nine patients with irresectable soft tissue tumors of the leg or arm have been treated with 0.2 mg gamma-IFN subcutaneously on the 2 days prior to ILP. ILP consisted of a 1½ hour perfusion with 0.2 mg IFN, 4 mg TNF (leg) or 3 mg TNF (arm), and 10 mg/L (leg)-13 mg/L (arm) limb volume of Melphalan at mild hyperthermia (39-40°C). There was extensive hemodynamic and cardiopulmonary monitoring perioperatively.
Results: Limb salvage was extraordinarily high in this group of patients with very large tumors. In the 29 pts. the perfusion therapy resulted in limb salvage in 27 pts (93%). Median follow-up 10 months (1-19 months). In 2 pts recurrent tumor or postoperative complications led to an amputation. There were no treatment related deaths.
Conclusion: ILP with high dosage TNF, IFN and melphalan appears to be very promising in achieving limb salvage in patients with irresectable extremity soft tissue sarcomas.

1018

RANDOMIZED PHASE II STUDY OF NEOADJUVANT CHEMOTHERAPY IN SOFT TISSUE SARCOMAS IN ADULTS. PROTOCOL 62874

GORTZAK E., ROUESSE J., VERWEY J., VAN GEEL A.N., BUESA J., SANTORO A., TURSZ T., VAN GLABBEKE M., KIRKPATRICKA., MOURIDSEN H.,

EORTC SOFT TISSUE AND BONE SARCOMA GROUP.

In April 1986 a randomized phase II study was activated in which high risk patients as defined by the EORTC Study 62771, i.e patients with larger sarcoma's; higher malignancy-grade, inadequately treated or with local recurrences were randomized between surgery +/- radiotherapy and 3 cycles in 9 weeks neo-adjuvant chemotherapy - adriamycin and ifosfamide before surgery +/- radiotherapy. Objectives of the study were to study accrual-rate and feasibility to determine the possibility of a phase III study, with as main interest to compare the diseasefree interval and survival.

105 patients were entered; 78 eligible, 16 not yet verifiable and 11 patients proved to be ineligible; male/female ratio 3:2; median age 50 years. Both arms are fairly balanced for stratification and localisation of the tumour. Local recurrence occurred in 9 patients without chemotherapy and in 4 patients in the chemotherapy-arm. 90 % of the patients completed 3 cycles of preoperative chemotherapy. 4 patients received only 1 cycle 1 due to neurotoxicity, 2 due to progression and 1 patient died of sepsis. 32 % responded with complete or partial remission; 50 % had stable disease before surgery. 4/31 (12%) showed progression. In both arms microscopically radical margins were obtained in 85 %. Postoperative morbidity was the same for infection, vascular or neurological complications as well as skin-necrosis.

Conclusion: the chemotherapy-regimen is feasible; longterm benefit is still to be assessed.

1019

THE VALUE OF POSITRON EMISSION TOMOGRAPHY (PET) IN DETECTION AND GRADING OF SOFT TISSUE SARCOMAS

H.Hoekstra, O.Nieweg, W.Molenaar, J.Pruim, J.Oldhoff, A. Willemsen, A.Paans, H.Schraffordt Koops, W.Vaalburg.

Dept's Surgical Oncology, Pathology, PET-center, Groningen University Hospital, Groningen, The Netherlands.

The value of PET with ^{18}F-fluorodeoxyglucose (FDG) was investigated in the detection and grading of fourteen soft tissue sarcomas (STS) of the lower extremity: 9 primary STS and 5 recurrent STS. The median tumor size was 10 cm (range 1.0 to 20.0 cm). An i.v dose of 370 MBq FDG was administered, and images were obtained with a Siemens ECAT 951 camera. After the PET scan all STS were excised. The glucose metabolic rate (MR_{gl}) was calculated in 10 pts; in 4 pts the MR_{gl} could not be calculated due to technical problems.
Results: Thirteen STS could be visualized with PET (93%); one recurrent grade I liposarcoma (10 cm) could not be detected.
The glucose consumption was expressed in μmol/100g/min. The mean MR_{gl} for grade I STS 3.8 (SD 0.6); grade II STS 15.5 (SD 8.0); grade III STS 27.8 (SD 11.3). The MR_{gl} difference between grade I and III STS was statistically significant ($p<0.01$).
Conclusion: The sensitivity of PET with FDG for the detection of primary and recurrent STS is high. PET has the ability for in vivo grading of low and high grade STS of the lower extremity.

1020

PHASE II STUDY WITH TAXOTERE(RP56976) IN ADVANCED SOFT TISSUE SARCOMAS OF THE ADULT.

OGCM van Hoesel, J Verweij, M Clavelt, G Catimel, P Kerbrat, NB Bui, J Kerger, AT van Oosterom, T Tursz, M van Glabbeke, C van Pottelsberghe, H Mouridsen for the EORTC Soft Tissue and Bone Sarcoma Group and N Le Bail for Rhone-Poulenc Rorer.

In a multi-center non-randomized phase II study Taxotere at a dose of 100 mg/m^2 in a 1-hour iv infusion q 3 weeks has been studied as a second line chemotherapy in advanced soft tissue sarcomas of the adult. Thirty patients (median age 54, performance status WHO 0: 13 pts, WHO 1: 13 pts, WHO 2: 4pts) were entered. Histological subtypes: malignant fibrous histiocytoma 5 pts, fibrosarcoma 1 pt, liposarcoma 5 pts, leiomyosarcoma 11 pts, rhabdomyosarcoma 1 pt, synovial sarcoma 2 pts, neurogenic sarcoma 2 pts, miscellaneous and unclassified sarcoma 3 pts. Twenty three patients are evaluable for response, 1 had early death due to malignant disease, 1 died due to toxicity and progression, 1 pt refused after 1 course, 8 pts are too early for evaluation. Five partial responses (5/23 = 21,7%, C.I. 7.46-43.70%) have been observed. In addition 1 patient experienced a mixed response. For toxicity 16 patients are evaluable : CTC grade ≥3 leucopenia occurred in 81.25% of patients and CTC grade ≥3 thrombopenia did not occur. Median nadir of neutrophils 0.23 $\times 10^9$/l. Episodes of fever and documented infection have been observed in 5 and 1 pts respectively. Anaphylactoid type reactions occurred in 1 patient. Peripheral neuropathy in 6/16 pts (CTC 1: 4pts, CTC 2: 2pts). Other adverse effects were skin reactions (pruritus, erythema and urticaria, CTC 1) in 8/16 pts. Peripheral edema believed to be related to anaphylactoid vascular leakage syndrome has been observed in 5/16 pts. One pt in partial remission went off study because of edema of the legs. Taxotere has activity in adult soft tissue sarcoma in second line, warranting studies on first line efficacy.

1021

SURGERY OF LUNGMETASTASES FROM SOFT TISSUE SARCOMA

AN van Geel [1], U. Pastorino, A. Pietraszek, P.I.M. Schmitz, on behalf of the EORTC Soft Tissue and Bone Sarcoma Group.

1 Dr Daniel den Hoed Cancer Center, Rotterdam, The Netherlands.

Retrospectively 161 patients with lungmetastases from soft tissue sarcoma treated surgically were studied. In all cases the metastasectomy was complete. The number of metastases removed was 1-13 (mean 3). Time between primary treatment and metastasectomy was 0-30 years (mean 3 years). Postthoracotomy follow-up ranged from 3 months - 20 years.
Overall survival was (3 years) 50%, (5 years) 38% and 10 years (27%).
Disease free survival after metastasectomy was (3 years) 40%,(5 years) 35% and (10 years) 26%.
Age at metastasectomy, disease free interval between initial treatment and metastasectomy, type, grade and site of the primary, number of metastases and access route to metastasectomy were analyzed as prognostic factors. In univariate analysis tumorgrade, number of metastases, disease free interval and radical resection have a significant influence on prognosis.
Results of multivariate analysis will be given.