arrest rather than tumour cell kill and thus early major changes in tumour volume are not to be expected. Assessment of tumour metabolic rate by PET has been suggested as an alternative end point for tumour response to therapy.

The **aim** of this study was to evaluate FDG-PET as an early metabolic response marker.

Methods: All patients (pts), included in EORTC phase I/II studies with STI 571, who underwent PET imaging prior to the start of treatment were included. All pts had histiological evidence of STS with documented progressive disease (PD). PET was performed prior to and 8 days after the start of treatment. PET consisted of an attenuation-corrected whole body scan acquired 1 hour after injection of FDG. Images were interpreted visually to assess the presence of new lesions and FDG uptake in target lesions was quantified (SUV_{max}). Four categories of metabolic tumour response (PD_{PET}, SD_{PET}, PR_{PET}, CR_{PET}) were defined based on the PET EORTC recommendations (*Young et al. Eur J Cancer 1999 1773–82*). Response on PET was correlated with subjective symptom control as well as objective tumour response evaluated on serial CT scans (RECIST criteria) acquired prior to and every 4 weeks after the start of treatment.

Results: At the time of writing, 24 pt were included (20 GIST, 4 other STS subtypes). In 2 GIST pts, the tumour was not FDG avid prior to treatment. Of the remaining 22 pts, CR_{PET} was seen in 10 pts and a clear PR_{PET} in 2 pts at day 8. All patients had major symptom relieve early after the start of treatment. Based on CT, objective tumour response (PR) was seen in 7/12 pts, however at later time points (3x at 4w, 3x at 8w, 1x at 16w). In the other 5 pts, categorised as SD according to RECIST criteria, treatment efficacy was presumed based on increased necrosis. SD_{PET} was found in 4 pts: 3 pts (1 non-GIST) still show SD on CT (FU 8m, 8w, 8w). In 1 pt, treatment was stopped after 8w because of increasing abdominal complaints and possible PD of the large abdominal mass on CT. PD_{PET} was seen in 6 pts (3 non-GIST) and a rapid increase in tumour-related symptoms was observed in 5 of them. CT confirmed PD in all 6 pts, 1 week to 1 month after the start of treatment.

Conclusion: PET seems to be a promising tool in the assessment of early tumour response. Treatment failure could accurately be predicted as soon as 1 week after the start of therapy. If response on PET also predicts survival remains to be answered.

113 ORAL

Second primary cancer after Ewing tumours - experience in 690 patients from a cooperative treatment study

M. Paulussen[1], S. Ahrens[1], M. Lehnert[2], P.A. Voute[3], A. Zoubek[4], H. Juergens[1]. *[1] University of Muenster, Dept. of Paediatric Haematology/Oncology, Muenster, Germany; [2] University of Muenster, Epidemiological Cancer Registry, Muenster, Germany; [3] University of Amsterdam, Dept. of Paediatric Oncology, Emma Kinderziekenhuis/Academic Medical Centre, Amsterdam, The Netherlands; [4] St. Anna Children's Hospital, Vienna, Austria*

Purpose: Treatment of Ewing tumour involves high cumulative doses of drugs capable of inducing second primary malignancies. The second cancer risk in a large cohort of consistently treated patients was analysed.

Patients and Methods: 690 Ewing tumour patients between 1992 and 1999 received local therapy, and vincristine, actinomycin D, doxorubicin, ifosfamide and/or cyclophosphamide, randomised with or without etoposide. Second cancer incidences were estimated by competing risk analyses, standardised incidence ratios (SIR) were compiled in comparison to cancer registry data.

Results: 6/690 patients have developed second primary malignancies at a median observation time of 32 months: ALL/NHL, 2, MDS/AML, 2, liposarcoma, 1, squamous cell carcinoma, 1. In comparison to the general population, SIR were increased more than 20-fold. The cumulative second cancer risk 5 years after diagnosis of the Ewing tumour was 0.0093 for the total group. Etoposide, and additional phase II high-dose therapy increased the risk to 0.0118 and 0.0398 after five years, respectively.

Conclusion: The risk of second primary cancers observed was in the expected range for cancer survivors. High-dose therapy, and less markedly, etoposide may contribute to the overall second cancer risk.

Supported by Deutsche Krebshilfe Grants DKH M43/92/J2 and DKH 70-2551 J3, and EU BIOMED Grants BMH1-CT92-1341 and BMH4-983956

114 ORAL

Consistent evidence of activity of ecteinascidin (ET-743) in pretreated, advanced soft tissue sarcoma (ASTS): results from a pooled analysis of three pivotal phase II clinical trials (p2ct) and safety profile of a 24 h infusion schedule

A. Le Cesne[1,2], J.L. Misset, G. Demetri, J.A. Lopez-Martin[4], J.Y. Blay[2], A. van Oosterom[2], I. Judson[2], E. Brain, A. Yovine, R. Maki, J. Gomez[4], C. Guzman[4]. *[1] Institute Gustave Roussy, France; [2] EORTC-STBSG; [3] and ET-743 Phase II Study Group, (Europe, USA); [4] PharmaMar, Spain*

From 1/99 to 1/01, 194 patients (pts) with pretreated ASTS have been registered in three pivotal P2CT assessing efficacy of ET-743, 1.5 mg/m2, 24 h iv infusion q3w.

Main Endpoints: objective response (OR) rate and progression free rate at 6 months (PFR6m). Inactive agents have shown a progression rate of 82% within the first 6-8 w and active agents in ASTS induce a PFR6m of 18% (ASCO 2001; #1413).

Results: 127 pts have been evaluable for activity (median follow-up: 6 m). Median age: 51 yrs (18-76). M/F ratio 1:1.3. PS (ECOG) 0: 49.3%, 1: 50.7%. Histology: LeiomyoS: 41%; lipoS: 14%; synovialoS: 11%. Number of involved organs: 1: 44%; 2: 35%; >2: 19%. Prior treatment: neo/adjuvant: 28%; 1: 54%; 2: 26%; >2: 10%.; Median treatment duration: 3 cycles (cy)(1-20). Proportion of pts receiving 6 or more cy: 25%. The OR rate is 9.4% (CI95%: 5.0-15.9%). Minor responses have been noted in 11 pts (8.7%). OR have been observed in leiomyoS (6 pts), lipoS (3), synovialoS (2) and not specified sarcoma (1). The median time to OR has been 3 m and median duration of OR has not been reached (1.5±8+ m). Progression rate after 2 cy: 43%. The median time to progression and median overall survival are 2.8 m (2.0-3.6) and 10.2 m (8.7-11.7) respectively. The 1 yr survival and PFR6m are 40% and 27.2% respectively. Safety profile of ET-743 is based on available information from 163 out of the 379 pts treated with this schedule (518 cy) in any of the seven P2CT conducted in several tumors. The identification of baseline and drug-induced cholestasis as risk factors for severe toxicity (T) led to an amendment in October 1999 (ASCO 2000; #727). Main T per pt after the amendment (91 pts, 266 cy): grade (G) 4 neutropenia: 14%; G3-4 thrombopenia: 12%; G3-4 anemia: 18%; hyperbilirubinemia: G1-2: 9%, G3: 2%; G1-2 alkaline phosphatase: 46%; G3-4 ALAT: 40%; G2-3 nausea: 30%; G3-4 vomiting: 7%; G2-3 asthenia: 30%. Major SAEs: febrile neutropenia: 17/379 pts (4.5%); rhabdomyolysis: 6/379 pts (1.6%); toxic deaths: 4/379 pts (1.1%). Drug related mortality rate has been 1.6% (2/124 pts) and 0.8% (2/255 pts) before and after the amendment, respectively.

Conclusions: ET-743 is a valid therapeutic option in pretreated ASTS, inducing a prolonged tumor control in one fourth of pts. The identification of risk factors for severe T has improved its therapeutic index.

115 ORAL

Functional outcome after preoperative isolated limb perfusion with rhTNFalpha/Melphalan for high-grade extremity sarcoma

P. Hohenberger, C. Kettelhack, A. Herrmann, P.M. Schlag. *Charite, Humboldt University, Di. of Surgery and Srugical Oncology, Berlin, Germany*

Objective: To analyse long-term limb salvage rate and functional outcome in patients undergoing isolated limb perfusion (ILP) for locally advanced, high-grade soft tissue sarcoma of the extremities.

Patients and Methods: 55 pts. with high-grade sarcoma of the lower limb underwent ILP with TNF alpha plus melphalan followed by radical tumor resection including vessel graft and/or free myocutaneous flaps. patients. Mean tumor size was 9.6 ± 5.5 cm. No postoperative radiotherapy was administered in patients undergoing R0 resection. The functional outcome was analysed by using the rating scale of the Musculo-Skeletal Tumor Society (MSTS, best/maximum score 30 points) and physical disability was assessed with the Toronto Extremity Salvage Score (TESS, best/maximum score 100). Median follow-up is 33 months (4 - 69+ months).

Results: 51/55 patients underwent tumor resection and a clear margins (R0) could be achieved in 47/51 (92%). Primary limb salvage was possible in 44/51 pts (88%) and three of the seven amputations were minor (forefoot or ray). Local recurrence developed in four pts. (8%) and could be resected for cure in three of them, however, another patient required amputation.

The proportion of patients returning to work was 62.5%. Functional analysis by the MSTS score showed a median of 24 points (80% of the best possible score, range, 15 - 30). Functional disability analysis by TESS score resulted in 83,7 points (range, 46.5 -100). It could clearly be shown