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Abstract 100009

**Regional hyperthermia (RHT) improves response and survival when combined with systemic chemotherapy in the management of locally advanced, high grade soft tissue sarcomas (STS) of the extremities, the body wall and the abdomen: A phase III randomized pros.**

*R.D. Issels, L.H. Lindner, P. Wust, P. Hohenberger, K. Jauch, S. Daugaard, U. Mansmann, W. Hiddemann, J. Blay, J. Verweij; GSF, Neuherberg, Germany; Klinikum Grosshadern Med. Ctr. Univ. of Munich, Munich, Germany; University Hospital Charite, Berlin., Germany; University Hospital Mannheim, Mannheim, Germany; Department of Pathology, Copenhagen, Denmark; Centre Leon Berard, Lyon, France; Erasmus University Medical Center, Rotterdam, The Netherlands*

**Background:** Patients (Pts) with locally advanced, high-grade STS are at significant risk for local failure and for metastasis. We evaluated the ability of RHT to improve the outcome in pts who are treated with neoadjuvant chemotherapy. **Methods:** Eligibility included pts with STS = 5 cm, grade II/III, deep and extracompartmental, stratified according to site (E = extremity vs. Non-E = body wall and abdomen). Pts were randomly assigned to systemic chemotherapy (etoposide 250 mg/m<sup>2</sup>; ifosfamide 6 g/m<sup>2</sup>; adriamycin 50 mg/m<sup>2</sup>) alone (EIA) or to systemic chemotherapy combined with RHT (EIA + RHT) administered for 4 cycles every 3 weeks both prior and after local aggressive therapy (surgery + radiotherapy), respectively. Primary endpoints were local progression free survival (LPFS) and disease free survival (DFS). Objective (CR + PR) response rate (ORR) evaluated after 4 cycles (EIA vs. EIA + RHT) was a secondary endpoint. A total of 340 pts was required to show an improvement in median LPFS of 19.2 mos for EIA + RHT (α = 5% type I, 20% type II error). **Results:** Pts characteristics were well balanced between treatment arms. After median follow-up of 24.9 months (mos) an intention-to-treat analysis showed a significantly superior DFS for pts who received EIA + RHT (n = 169) compared to those treated with EIA alone (n = 172) (median DFS: 31,7 mos and 16,2 mos; log-rank p=0.003; Hazard ratio = 0.65; C195 = 0.48 – 0.87, p=0.004). The median LPFS was estimated 45,3 mos for EIA + RHT and 23,7 mos for EIA (log-rank p = 0.015; Hazard ratio = 0.66; C195 = 0.48 – 0.90, p = 0.01). At 2 years, LPFS rates for E (149 pts) and for Non-E (192 pts) were significantly better for EIA + RHT vs. EIA alone (E: 84% vs. 64%; Non-E 57% vs. 39%) (p<0.02). The ORR was significantly better for EIA + RHT (28,7%) vs. EIA alone (12,6%) (p=0.002). **Conclusions:** Compared to chemotherapy alone, RHT combined with chemotherapy yields a statistically significant improvement in tumor response, DFS and LPS, in patients with locally advanced, high-grade STS. (Supported by Deutsche Krebshilfe and HGF VH-VI-140).