

**RISK OF EARLY PROGRESSION IN PATIENTS WITH HIGH-RISK SOFT
TISSUE SARCOMAS: RESULTS OF THE PHASE III RANDOMIZED
PROSPECTIVE TRIAL OF NEOADJUVANT
CHEMOTHERAPY WITH OR WITHOUT REGIONAL
HYPERTHERMIA (EORTC-ESHO INTERGROUP TRIAL)**

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Background:

A randomized phase III trial of neoadjuvant chemotherapy combined with or without RHT for pts with locally advanced high grade STS was recently completed (Issels, ASCO 2007). By interim analysis the overall risk of early progression (PD) during the 3-months duration of neoadjuvant chemotherapy with or without RHT was 15% (Lindner, ASCO 2005, #9020). We now analyzed the risk of early PD for both treatment arms including subgroup analysis for pts with not operated primary (S1) or recurrent (S2) STS and for pts after R1/R2 resection of primary or recurrent STS (S3).

Methods:

From 7/97-11/06 341 pts (S1=161; S2=37; S3=143) with STS > 5 cm, grade MII, deep and extracompartmental have been randomized to receive initially 4 cycles of systemic chemotherapy (etoposide 250 mg/m²; ifosfamide 6 g/m²; adriamycin 50 mg/m²) alone (EIA) or systemic chemotherapy combined with RHT (EIA + RHT). Early PD was defined as local and/or distant relapse or any kind of death after 3 and 6 months, respectively. By intention to treat analysis the risk of early PD was assessed for all randomized 341 pts after a median follow up time of 25.5 mths.

Results:

The local progression free survival (LPFS) for EIA+RHT vs. EIA alone after 3 mths was 94.6% vs. 86.0% (Diff. = 8.6%, CI95= 2.3-14.9%, p=0.008) and after 6 mths 91.4% vs. 77.8% (Diff. = 13.6%, CI95= 5.9-21.3%, p<0.001). The disease free survival (DFS) for the EIA+RHT vs. EIA alone after 3 mths was 94.0% vs. 83.1% (Diff. = 10.9%, CI95= 4.1-17.6%, p=0.002) and after 6 mths 87.7% vs. 73.8% (Diff. = 13.9%, CI95= 5.5-22.3%, p=0.001). For the S1/S2 subgroup the LPFS for EIA+RHT vs. EIA alone after 3 mths was 90.5% vs. 81.0% (Diff.=9.5%) and after 6 mths 85.0% vs. 73.4% (Diff. = 11.4%). For the S3 subgroup the LPFS for EIA+RHT vs. EIA alone after 3 mths was 100% vs. 92.8% (Diff.=7.2%) and after 6 mths 100% vs. 83.8% (Diff.=16.2%).

Conclusions:

Compared to chemotherapy alone, the risk of early PD for all patients is significantly lower for the hyperthermia combined chemotherapy regimen irrespective of time point of surgery.

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