

NEOADJUVANT CHEMOTHERAPY ± REGIONAL HYPERTHERMIA (RHT): LOCAL CONTROL AND PROGRESSION FREE SURVIVAL OF 122 PTS WITH HIGH-RISK SOFT TISSUE SARCOMAS (HR-STs) AFTER PREVIOUSLY INADEQUATE SURGERY TREATED WITH

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Introduction

Positive margins after initial surgery of large (≥ 5 cm), high grade and deep HR-STs is a known risk factor for local recurrence and critical for local progression free survival. Beside primary (S1-group) or recurrent (S2-group) HR-STs the EORTC 62961/ESHO RHT 95 intergroup phase III study is recruiting also pts with HR-STs after initial inadequate surgery (S3-group). Therefore we analyzed local control and progression free survival for this subgroup of pts with comparison of outcome to the other both subgroups.

Methods

Among 291 pts (340 pts planned) with HR-STs randomized between 7/97 – 10/05, 122 pts, median age 51 yrs (range 18-69 yrs), primary median tumor diameter 9 cm (range 5-36 cm), all high grade, and extracompartmental entered the protocol after previously inadequate surgery (close margins: < 10 mm or macroscopic residual tumor). The protocol prescribed 4 pre- and 4 postoperative cycles EIA (total dose per cycle: etoposide 250 mg/m²; ifosfamide 6 g/m²; and doxorubicin 50 mg/m²) either combined with RHT (60 min, $T_{\max}(\text{tumor}) = 42.5^{\circ}\text{C}$) parallel to EIA or EIA alone. In case of measurable tumor, response evaluation and definitive surgery and/or adjuvant radiotherapy were assessed for each patient after the first 4 cycles EIA ± RHT. All pts entering the protocol with primary (S1=137 pts), recurrent (S2=32 pts) or with inadequate resected tumors (S3=122 pts) were stratified to extremity (E=126) or non-extremity (NON-E=165).

Results

For response evaluation of patients with measurable disease after inadequate surgery (41/122) the clinical objective response rate to the neoadjuvant chemotherapy ± RHT (3 CR/10 PR) was 32%. The other pts showed stable disease (2 MR, 21 NC) (56%) or progression of disease (5 PD) (12%). For the 122 pts the 3-year local progression free survival (LPFS) was 60.4% (95% CI 49.9-71%) and - according to site - for E (43 pts) 86.3% (95% CI 74.7-97.8%) and for NON-E (79 pts) 48.3% (95% CI 35.6-61.6%), respectively.

Conclusions

Patients with inadequate surgery (S3) showed a higher objective response rate (32%) if compared with the overall response rate (23%) seen in all 291 pts (S1+S2+S3). Local progression free survival at 3 years for this subgroup was comparable for E (S3=86.3% vs S1 + S2=85.4%) but significantly better for NON-E (S3=48.3% vs S1+S2=33.2%; $p < 0.05$). These pts do obviously benefit from the subsequent treatment regimen despite the high risk for local failure.