# FDG PET-CT RESPONSE AFTER NEOADJUVANT CHEMOTHERAPY CONTINUES TO PREDICT PROGRESSION FREE SURVIVAL AT MID-TERM IN PROSPECTIVE TRIAL FOR SOFT TISSUE SARCOMAS

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ABSTRACT BODY:
Objective: Surrogate endpoints are needed to allow rapid study of new agents without doing lengthy trials using the gold standard endpoint of survival. Noninvasive assessment of treatment response is needed to guide treatment & tailor surgical margins. We previously presented this trial's initial interim analysis correlating PET-CT with histologic response after chemotherapy (CTOS 2009) & now present longer-term results. The primary aim of this prospective trial (NCI # NCT00346125) was to correlate PET-CT with progression free survival (PFS) & secondarily to analyze PET-CT change over time with serial imaging.

Methods: Patients with high grade soft tissue sarcomas > or = 5 cm enrolled in a prospective trial using ifosfamide/doxorubicin (4 cycles) before tumor excision. PET-CT was done at baseline, after cycle 1, & just before surgery. ΔSUVmax change (baseline to after cycle 1[B-1] & baseline to surgery [B-S]) was tested as a predictor of PFS using Kaplan-Meier estimates & Cox regression. PET-CT response was defined as ΔSUVmax reduction ≥40%. Serial ΔSUVmax was analyzed to assess chemotherapy impact over successive cycles.

Results: Of 69 patients enrolled, 52 completed the protocol & are under disease surveillance. Mean follow-up duration = 41 months (3.6 - 78.4 months). Patients with PET-CT response [B-S] had significantly longer PFS: 3 yr (76%, 95%CI: 54-88%) vs non-responders (27%, 95%CI: 7-54%), p=0.0022, Figure 1; 5 yr (65%, 95%CI: 42-81%) vs non-responders (27%, 95%CI: 7-54%), p=0.0063, Figure 2. After 1 chemo cycle (PET-CT response [B-1]), ΔSUVmax still predicted PFS (p=0.035) at 3 years & (p=0.012) at 5 years. Upon Cox regression, PET-CT response (either continuous measurement [B-S] or categorical variable [cutoff at 40%]) was predictive of PFS (p=0.0056 and p=0.016, respectively), even when adjusted for age, baseline tumor volume, AJCC stage, radiation (yes/no) and chemotherapy (complete/incomplete). SUVmax decreased significantly over time (p<0.0001) with greatest reduction after chemo cycle 3 compared separately to cycles 1 and 2 (p<0.0001, p<0.0072 respectively).

Conclusion: ΔSUVmax on FDG-PET-CT after neo-adjuvant chemotherapy independently predicted PFS. This supports using FDG-PET-CT as a proxy of both histologic response and PFS as well. FDG-PET-CT may have both a clinical role in the prediction of chemotherapy efficacy, as early as after 1 cycle, and a research role as a survival endpoint proxy, thus facilitating rapid assessment of new targeting therapies in clinical trials.

**Figure 1:**

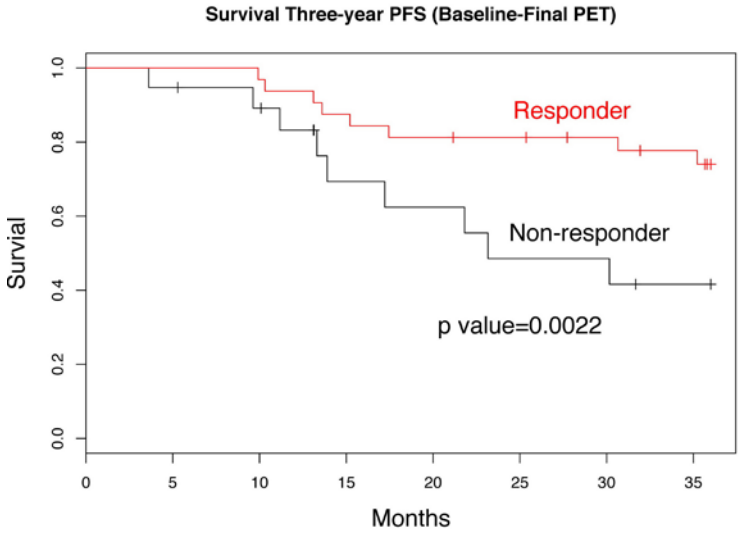


**Figure 2:**