

PREDICTING RESPONSE TO NEOADJUVANT CHEMOTHERAPY IN INVASIVE BREAST CANCER: GENE EXPRESSION PROFILING OF PARAFFIN-EMBEDDED CORE BIOPSY TISSUE

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Rationale: Quantification of tumor gene expression may provide more precise characterization of breast cancer and guide chemotherapy to maximize patient benefit and minimize toxicity.

Methods: Patients (pts) with newly diagnosed stage II or stage III breast cancer were treated with sequential doxorubicin 75 mg/M² q2 wks x 3 and docetaxel 40 mg/M² weekly x 6; treatment order was randomly assigned. Fixed paraffin-embedded (FPE) tissues were obtained prior to and after chemotherapy (CTx). A validated high throughput RT-PCR assay is used to quantitate expression of 7 reference genes and 185 cancer-related genes. The latter were selected by review of the published literature and DNA microarray experiments.

Results: To date, RNA has been extracted from FPE tumor tissue in 31 pts (planned study size 69 pts). Pre-CTx specimens were obtained by core biopsy in 24 pts and by incisional biopsy in 7 pts. Of note, sufficient RNA for quantitative analysis of expression for 192 genes (> 0.5 ug) was obtained in 22 of the 24 pre-CTx core biopsies. Total RNA yield from six 5 sections of the core biopsy tumor blocks was 7.0 ± 6.7 ug (mean SD, n = 24) (range 0.2 - 27.7 ug). Thus far, quantitative gene expression for 192 genes has been performed in 4 core biopsy pre-CTx pts. RT-PCR results for ER expression were high in 2 of these pts (2.5-fold and 13-fold higher than the average of the reference genes) and low in the other 2 pts (11-fold and 18-fold lower than the average of the reference genes). These results are consistent with ER status as determined by IHC, and indicate the large dynamic range of the RT-PCR assay. The RT-PCR assay will explore the correlation between pre-CTx gene expression and tumor response, and characterize differences between pre-CTx and post-CTx gene expression.

Conclusion: Sufficient RNA is obtained from fixed paraffin-embedded core biopsy tumor tissue for quantification of expression of 185 candidate gene markers for correlation with neoadjuvant CTx response. Detailed analysis of the correlations between quantitative gene expression and response will be presented.