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Determining Relevant Biomarkers from Tissue and Serum that May Predict Response to Single Agent Lapatinib in Trastuzumab Refractory Metastatic Breast Cancer.

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Abstract: **Background:** Lapatinib is an oral tyrosine kinase inhibitor that potently inhibits both ErbB1 and ErbB2 tyrosine kinase activity. Results of two Phase II trials in metastatic breast cancer (MBC) suggest activity of lapatinib in trastuzumab (T) pretreated patients. The main objective of this report was a combined biomarker analysis from these two large studies to evaluate correlations between clinical parameters, tissue/serum biomarker expression and response to lapatinib. **Methods:** Eligible patients had MBC with disease progression following T-containing regimens in the 1st phase II study and were anthracycline, taxane, capecitabine and T exposed in the 2nd phase II study. Tumor tissues were obtained on each patient from the time of most recent biopsy. Using standard IHC techniques, tumors were stained for: ErbB1-4, IGF1R, truncated ErbB2 (p95), heregulin and p-Erk 1/2. Sequential quantitation of extra-cellular domain (ECD) for both ErbB1 and ErbB2 were obtained. **Results:** Investigator reported efficacy data on the first 81 patients from the combined trials demonstrates a total of 19 patients progression-free at 16 weeks of which 7 achieved an objective response (CR or PR). The mean T exposure in the 1st study was 46 weeks and in the 2nd study 84 weeks. As of Dec 2004, both studies have completed accrual with a total of 215 patients. For the initial 37 tumors analyzed, IHC data indicate only 6/37 patients overexpressed both ErbB1 and ErbB2. To date, over 100 tumor tissues have been collected and tested for ErbB1-4, IGF1R, p95, heregulin, and p-Erk 1/2. Initial data suggest that expression levels of ER, PR and ErbB1 may be related to lapatinib response in T pre-treated patients. Declines of ErbB2 ECD at both week 4 and week 8 appear to predict response to lapatinib. A multivariate analysis for response

predictors, including all collected tumors, sequential ECD levels and clinical parameters will be performed. **Conclusions:** Inhibition of both ErbB1 and ErbB2 with lapatinib represents a promising approach in the treatment of MBC. This analysis of potential predictive molecular phenotypes for response to lapatinib in T-resistant tumors will be the most extensive to date.

Associated Presentation(s):

1. Determining relevant biomarkers from tissue and serum that may predict response to single agent lapatinib in trastuzumab refractory metastatic breast cancer

Event: 2005 ASCO Annual Meeting

Presenter: [Kimberly L Blackwell, MD](#)

Session: The Challenge of Trastuzumab Resistance

