Supplementary Tables:

Supplementary Table 1: Toxicities: incidence and National Cancer Institute (NCI) CTC grading

Supplementary Table 2: Biomarker changes in placebo treated arm. Pre-treatment and surgical protein and mRNA expression biomarker values for control placebo-treated patients, together with percentage change and p-values showing the statistical significance of the change. Geometric means and 95% confidence intervals are shown, except for HER2 FISH (Median,CI) and EGFR (% not negative), ’na’ indicates not assessable, in these instances there are too few patients for the analysis to be performed.

Supplementary Table 3: Correlation between baseline protein and mRNA expression biomarker values with Ki67 response (defined as >50% fall in Ki67). A logistic regression was performed to assess the ability of each baseline biomarker, treated as a continuous factor, to predict a fall in Ki67 of 50% or more, (+) indicates the direction is for higher biomarker values to increase the likelihood of response, (-) indicates that a low value increases the likelihood of Ki67 response. ’na’ indicates there are too few patients for the analysis to be performed. Protein expression was assessed by IHC and mRNA by RT-PCR.

Supplementary Table 4: Correlation of change in protein and mRNA biomarker values with change in Ki67 for both lapatinib-treated and placebo-treated control patients. Spearman rank correlation is shown. Protein biomarkers in this table were assessed by IHC, and mRNA expression by RT-PCR.

Supplementary Figures:

Supplementary Figure 1 : Correlations between expression levels of ER, PgR, HER2 or EGFR and Ki67 in baseline tumor samples

Supplementary Figure 2 : Change in Ki67 with Lapatinib in HER2-ve group according to HER2 mRNA and HER3 mRNA expression

Supplementary Figure 3 : Correlations between Ki67 response and expression of epiregulin in HER2+ lapatinib-treated cases