patients with relative dose intensity (RDI) ⩾ 85%, with secondary objectives of incidences of dose delays and dose reductions due to neutropenic events, toxicity and disease free survival.
Results: Between May 2005 and May 2006 51 pts were recruited (25 Arm A, 26 Arm B). Baseline demographics and disease characteristics are shown in the table, as is RDI and the incidence of hematological toxicities.
Conclusions: In this study, proportion of patients with RDI ⩾ 85% was 96% and 89% in pegfilgrastim augmented dose-dense FEC75 and FEC90 arms. No patient experienced febrile neutropenia and there were only single occurrences of grade 3−4 leukopenia and neutropenia. Thus, within the short time period assessed, these initial data suggest that both regimens are safe in the adjuvant treatment of early breast cancer.

Oral presentations (Tue, 25 Sep, 09.00−11.00)
Breast cancer – advanced disease

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Lapatinib (L) plus Capecitabine (C) in HER2+ advanced breast cancer (ABC): report of updated efficacy and gene-array data

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Background: EGF100151 demonstrated L+C improved TTP relative to C alone in women with HER2+, trastuzumab-exposed ABC [Geyer, NEJM 2006; 355(26)]. We report updated efficacy results and correlative studies to determine if differential gene expression levels are associated with clinical benefit of L+C.
Methods: Tumor blocks were available for 217/399 patients; sufficient mRNA was extracted from103/217 patient tumor blocks for evaluation of gene expression by qRT-PCR and by Affymetrix HU133 plus 2.0 gene expression arrays. SpotFire™ DecisionTree analysis was performed on the qRT-PCR data to determine the genes significantly associated with RR; genes were further analyzed for association with TTP using Kaplan Meier survival analyses. Preliminary gene array data were analyzed, to date only in the combination arm, using a Wilcoxon's test (cut-off $p < 0.01$) to determine genes with significant differential expression between the responders and non-responders.
Results: Efficacy results as of April 3, 2006: TTP L+C 27 wk vs C 19 wk, HR 0.57 [0.43, 0.77], $p = 0.00013$; ORR L+C 24% vs C 14%, Odds Ratio 1.9 [1, 1.34], $p = 0.017$; OS L+C vs C HR 0.78 [0.55, 1.12], $p = 0.177$; progression in CNS L+C 2% vs C 11%, $p = 0.0445$. Amongst 103 patients with mRNA data, there were 19 responders (PR = 19), 26 non-responders (SD = 20, PD = 6) and NE = 10 in L+C; 5 responders (PR = 5), 22 non-responders (SD = 20, PD = 12) and NE = 8 in C. Preliminary analysis of gene array data show elevated baseline HER2 mRNA expression correlates with response to L+C ($p < 0.01$) in L+C. This finding was confirmed by qRT-PCR data where elevated baseline HER2 mRNA expression is associated with higher RR as well as longer TTP ($p < 0.0001$) with L+C. In addition, gene array data revealed that patients with elevated baseline FOX3A mRNA levels and reduced baseline BCL-2 mRNA responded to L+C in the combination arm alone; consistent with preclinical response data in breast cancer cell lines.
Conclusion: Updated efficacy results confirm the prior demonstrated benefit of L+C vs C and provide evidence for systemic anti-HER2 therapy effects on the development of CNS metastases. Preliminary data suggest a correlation between elevated HER2 mRNA levels and RR/TTP. In addition, preliminary gene array data suggest that patients whose tumours have increased regulation of HER signaling and induction of apoptotic pathways gain greater clinical benefit from treatment with L+C. Additional array analyses will be discussed from both treatment arms.

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Biomarker analysis of lapatinib with paclitaxel versus paclitaxel as first-line treatment in 580 patients with metastatic breast cancer

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Background: Lapatinib is an oral tyrosine kinase inhibitor of EGFR/HER2 that was recently approved in US for use in combination with capecitabine for HER2-overexpressing (HER2+) advanced/metastatic breast cancer (BC) pretreated with taxanes, anthracyclines, and trastuzumab-based therapy. Paclitaxel has shown activity alone and in combination for HER2+ BC. We report here an analysis on HER2, ER, and PR for 580 patients (pts) with incurable Stage IIIb/IIIc/IV BC at first diagnosis or relapse whose HER2 status was unknown or negative (IHC0/1+ or FISH−) at study entry.
Methods: Between Jan 2004 and Jul 2005, 580 first-line pts from 24 countries were stratified by metastatic site and randomized 1:1 to 1500 mg lapatinib QD + 175 mg/m^2 paclitaxel q3w or placebo QD + 175 mg/m^2 paclitaxel q3w. Primary endpoint was TTP; secondary endpoints were AEs, ORR, PFS, CBR, RFS, and OS. Archived tumor tissue and/or slides obtained from the most recent biopsy were centrally analyzed in blinded fashion for HER2 (IHC and FISH) and ER/PR (IHC). Based on these results, pts were categorized into 3 groups: HER2+, luminal, and basal.
Results and Conclusions: Biomarkers were correlated with clinical efficacy in 579 pts; 542 (93%) pts had tissue available for central analysis. 91 (18%) pts were determined to be HER2+ by FISH or IHC3+. In the HER2+ subset, a statistically significant improvement was observed in lapatinib + paclitaxel vs paclitaxel-treated patients in both median TTP (35.1 v 25.1 wks, HR = 0.57, 95% CI 0.34, 0.93, $p = 0.0107$) and ORR (59.6% v 35.9%, odds ratio=2.9, 95% CI 1.1, 7.9, $p = 0.027$). Efficacy data in subgroups of patients based on hormone receptor expression levels and breast cancer subtype will be reported. Overall survival data will be available at the time of presentation.
In conclusion, lapatinib in combination with paclitaxel demonstrated statistically significant clinical activity as measured by TTP/PFS and ORR in a targeted population of HER2+ pts with metastatic BC.

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BCIRG 007: First overall survival analysis of randomized phase III trial of trastuzumab plus docetaxel with or without carboplatin as first line therapy in HER2 amplified metastatic breast cancer (MBC)

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Background: Based on preclinical synergism between docetaxel (T), carboplatin (C) and trastuzumab (H), BCIRG conducted a phase III trial in HER2-positive MBC to evaluate efficacy and safety of H in combination with T or TC.
Methods: 263 patients (pts) with HER2 FISH+ MBC were randomized to TH (H with T 100 mg/m^2) or TCH (H with T 75 mg/m^2 and C AUC=6). Chemotherapy was given every 3 weeks (q3w) for 8 cycles with weekly H at 2 mg/kg (loading dose of 4 mg/kg) followed by H q3w at 6 mg/kg until progression. Pts were stratified by centre and prior (neo) adjuvant taxane chemotherapy. Primary endpoint was Time To disease Progression (TTP). Secondary endpoints include overall survival, response rate, duration of response (DR), clinical benefit (CB) and safety. In addition, a sub study on Serum HER2 Extra Cellular Domain (ECD) was conducted on the 89% of subjects with levels >15 ng/mL at the time of metastatic disease (86% in TH-treated subjects vs. 92% in TCH-treated subjects).
Results: 131 pts were treated in each arm Pt characteristics were well balanced in both groups. A first efficacy analysis was conducted at 204 events. There was no significant difference between TH and TCH in median TTP (11.1 vs 10.4 mos, $p = 0.57$), ORR (73% in both arms), DR (10.7 vs 9.4 mos) and CB (67% in both arms). At 39 months of median follow-up, median overall survival was 36.40 and 36.57 months in TH and TCH arms respectively. More patients on TCH received the max number of chemotherapy cycles, and numerically fewer patients on TCH discontinued treatment as a result of non hematological toxicity. The most common gr 3/4