significantly different: grade 3/4 toxicities were more pronounced in CD arm; diarrhea (GD = 8%; CD = 18%; p = 0.0088), mucositis (GD = 4%; CD = 15%; p = 0.0008), and hand-foot syndrome (GD = 0%; CD = 26%; p < 0.0001). 13% of pts stopped therapy due to adverse event on GD vs 30% on CD. Best overall response rates in both arms were 32% (p = 0.93). Median PFS (1% of patients censored in GD and 7% in CD) was 8.05 months (95% CI 6.60–8.71) in GD arm, and 7.98 (95% CI 6.93–8.77) in CD arm (log-rank p = 0.121). Of notice when interpreting this data, 11% in GD arm vs 26% in CD arm received additional chemotherapy before progression. With a median follow-up of 19.2 months, and 23% of patients censored, the median overall survival was 19.29 months (95% CI 15.57–23.59) on GD arm, and 21. 45 (95% CI 17.12–24.94) on CD arm (log-rank p = 0.982).
Conclusion: These data suggest that the two regimens are comparable in efficacy; however a more favorable toxicity profile on GD arm may be a determining factor in selecting a better treatment option. Exploratory sub-group efficacy analysis results will be presented at the meeting.

O-50 Role of Caveolin-1 expression in docetaxel resistance in breast cancer cells

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Docetaxel is very effective in the treatment of breast cancer. However, despite its efficacy, resistance to docetaxel remains a significant problem and the genetic pathways involved in docetaxel resistance are not well understood. We have previously used comparative genomic hybridization (CGH) and bacterial artificial chromosome (BAC) fine-mapping on docetaxel resistant breast cancer cell lines to identify and accurately map the minimal chromosomal regions that are modified in docetaxel-resistant cells relative to their parental docetaxel-sensitive cells. Caveolin-1 is one of the candidate genes identified by CGH and BAC-mapping to be amplified in docetaxel-resistant MDA-MB-231 cells. The role of caveolin-1 in docetaxel resistance was investigated by modulating its expression in these cells.
Caveolin-1 protein expression in docetaxel-resistant cells relative to parental, docetaxel-sensitive cells was analysed by western blot analysis. Caveolin-1 siRNA or scrambled control siRNA was transfected into docetaxel-resistant cells and mRNA knockdown was monitored by RT-PCR. MTT cytotoxicity assay was used to monitor effects on docetaxel resistance in the transfected cells.
Caveolin-1 protein expression in docetaxel-resistant cells was found to be increased 5.96-fold ($\pm$1.63) relative to docetaxel-sensitive cells. Complete knockdown of caveolin-1 mRNA expression was achieved in docetaxel-resistant cells transfected with caveolin-1 siRNA compared to scrambled control siRNA, 48 hours post-transfection. Pilot data from MTT assays demonstrated an increase in sensitivity in caveolin-1 siRNA transfected cells compared with control siRNA transfected cells, at lower concentrations of docetaxel
This preliminary study highlights that overexpression of caveolin-1 may be involved in resistance to lower concentrations of docetaxel in MDA-MB-231 breast cancer cells.

O-51 Expression of thioredoxin system proteins in locally advanced breast cancer – correlations with response to anthracycline based chemotherapy (C/T).

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The thioredoxin (Trx) system helps maintain a reducing environment in cells and regulates many key biologic processes including cellular growth, transcription factor activity, acting as an antioxidant and regulator of apoptosis. Expression of thioredoxin binding protein (TXNIP), a negative regulator of Trx, is frequently lost in tumor tissues and cell lines. Thioredoxin over expression is associated with resistance to several chemotherapeutic agents *in vitro*.
The present study examined, in 60 locally advanced breast cancer patients treated by FEC/FAC for 4–6 cycles in the neoadjuvant setting, whether the expression of Trx and related proteins (TXNIP and thioredoxin reductase, TrxR) were associated with resistance to C/T. Standard immunohistochemical techniques were used to assess protein expression both pre- and post C/T and results correlated with clinical response.
Tumours with high pre-C/T Trx and TrxR expression showed a lower complete response rate (CRR) than those with low expression ($P < 0.05$). High expression of TXNIP also correlated with a higher CRR. Trx expression significantly increased after anthracycline therapy (24.5% increase; $P < 0.001$). There was no significant increased expression of either TrxR or TXNIP following C/T. Tumors with high Trx expression showed significantly lower TXNIP expression and vice versa. We conclude that Trx and TXNIP may be clinically useful biomarkers for predicting response to anthracycline based C/T and that if using Trx expression to monitor response then TXNIP should also be assessed.

O-52 The basal phenotype (BP) is highly expressed in locally advanced breast cancer (LAPC) but does not predict response to neo-adjuvant anthracycline based chemotherapy

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Background: The prognostic value of BP is well established. This study aimed to investigate the incidence of BP in LAPC and evaluate it as a marker for predicting response to neo-adjuvant anthracycline based chemotherapy.
Methodology: The study involved 60 LAPC patients at Nottingham City Hospital treated with 6 cycles of FEC/FAC neo-adjuvant chemotherapy between December 1996 and January 2007. A pragmatic definition of BP as immunophenotypic evidence of basal cytokeratins CK5/6 and/or CK14 expression was used. Standard immunohistochemical techniques were employed to assess marker expression in pre-chemotherapy core biopsies and results correlated with clinical response (RECIST).
Results: Of 60 cores stained, 34 (56%) were BP positive. 20 of them were also ER negative (33% overall). The BP positive subgroup (34/60) responded as follows: 30 responders (88%) (15 CR and 15 PR) versus 4 non-responders (12%) (3 SD and 1 PD). In the BP negative subgroup (26/60), there were 22 responders (84%) (10 CR and 12 PR) versus 4 non-responders (16%) (3 SD and 1 PD). 14 of the 60 (23%) patients suffered recurrences: 10 (71%) were BP positive while 4 (29%) were negative. Of other response predictors such as Her2/Topo2α, Ki67 and p53, only Ki67 negativity predicted resistance in this cohort (p = 0.007).