category. The 10-year RFS of a patient with a BMI of 25 kg/m^2 vs. one with a BMI of 35 kg/m^2 was approximately 70% vs. 65%.

Table 1. Relapse Free and Overall Survival by BMI

BMI (kg/m^2)	N	RFS (%)		OS (%)	
		5 year	10 year	5 year	10 year
<25	642	80.9	71.4	87.7	76.9
25.0–29.9	628	75.5	66.5	84.1	70.6
⩾30	636	74.9	65.0	82.7	69.8

Conclusions: We found a modest linear relationship between BMI and outcome in node-positive breast cancer patients receiving chemotherapy. Obesity, an increasing public health concern, is a modifiable factor; additional research is needed to determine the impact of weight loss on breast cancer outcomes.

414 Proffered paper oral

Variations in the Prevalence of Risk Factors for Breast Cancer in Different Ethnic Groups in the Million Women Study

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Background: The Million Women Study is a large prospective study in the United Kingdom (UK), designed to investigate the health of women, with a focus on breast cancer. There are known differences in the incidence of breast cancer in different ethnic groups in the UK, but information about the risk factors for the disease in these ethnic groups is limited. The aim of this study is to describe the distribution of known risk factors for breast cancer by ethnic origin in this cohort.

Materials and Methods: UK women aged 56 years, on average, were recruited into the Million Women Study between 1996 and 2001. Information about risk factors and potential confounders for breast cancer and other diseases were collected using self administered questionnaires. Participants of the study are linked to routinely-collected national databases, such that information on incident cancers and hospital admissions are notified automatically to the study investigators.

Results: Of the 1.1 million women in the study with a recorded ethnicity, almost 8000 women were Asian and almost 5000 women were Black. On average, Black women had 3.1 children, compared to 2.9 children for Asian women and 2.4 children for white women. The prevalence of having ever breastfed amongst parous women was lower for white women (69%) than for Asian (83%) or Black (83%) women. The mean body mass index was higher for Black women (28.1 kg/m^2) compared to Asian (26.0 kg/m^2) and white (26.2 kg/m^2) women. Never use of alcohol was much more common amongst Asian (70%) than Black (38%) or white women (23%). Current HRT use was higher for white women (35%), compared to Black (29%) and Asian (24%) women. 10% of white women had a first degree relative with breast cancer, compared to 8% of Black women and 6% of Asian women. A much higher prevalence of social deprivation was found in Black and Asian women than in white women with 55% of Blacks, 43% of Asians and 19% of whites in the lowest socio-economic quintile. All these differences were highly statistically significant ($P < 0.001$).

Conclusion: The Million Women Study provides a unique opportunity to compare the health of women of different ethnic origins in the UK. These results show substantial and significant differences in the risk factors for breast cancer between middle-aged Black, Asian and white women in the UK. Further analyses will be done comparing differences in the incidence and management of breast cancer in women by ethnic origin, allowing for their large differences in risk factors for the disease.

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Genetic Variability in Multi Drug Resistance Protein 1 (ABCC1/MRP1) and UDP-Glucuronosyltransferase-2B7 (UGT2B7) Are Highly Correlated with Severe Haematological Toxicity of Adjuvant FEC in Breast Cancer

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Background: We assessed the impact on hematological chemotherapy toxicity of single nucleotide polymorphisms (SNP) in germline DNA in a panel of potential genes of interest through high throughput sequencing. First aim was to validate the predictive value of certain SNP that have previously been shown to correlate with toxicity/outcome in small patient groups receiving at least one of the FEC compounds (ABCBI/MDRI, ABCC1/MRP1, ABCC2/MRP2, ABCG2, ALDH3A1, CYP2B6, CYP2C8, CYP2C9, CYP2C19, CYP3A5, DPYD, GSTP1, MTHFR, NQ01, TYMS, XPD/ERCC2, XRCC1). Secondly we investigated previously not studied genes known to be involved in epirubicin metabolisation (UGT1A1, UGT1A6, UGT2B7).

Material and Methods: We identified 1089 breast cancer patients treated in a single centre with 3 to 6 cycles of (neo-)adjuvant FEC (fluorouracil 500, epirubicin 100, cyclophosphamide 500 mg/m^2) from 2000–2010 for whom germline DNA is available. All patients were retrospectively evaluated through electronic chart review for febrile neutropenia (primary endpoint), febrile neutropenia first cycle, prolonged grade 4 or deep (<100/μl) neutropenia, anemia grade 3−4 and thrombocytopenia grade 3-4. For statistical evaluation, correction was made for number of planned cycles, primary growth factor use, age and body mass index. Because of multiple testing the false discovery rate (FDR) was calculated.

Results: Variant genotypes for rs45511401 (GT/TT, 12%) in the Multi Drug Resistance Protein 1 gene (MRP1/ABCC1), compared to the wild-type (GG, 88%) were associated with febrile neutropenia, febrile neutropenia in first cycle and thrombocytopenia (respectively 26.5 vs 15.8%, 17.1 vs 9.7% and 3.4 vs 0.3%; p-value 0.007, 0.027 and 0.005, FDR 0.3, 0.79 and 0.19). Variant genotypes for rs7668282 (CC/CT, 1.5%) in the UDP-Glucuronosyltransferase 2B7 gene (UGT2B7) compared to the wild-type (TT, 98.5%) genotype were associated with febrile neutropenia and prolonged or deep neutropenia (respectively 6.7 vs 17.2% and 6.7 vs 35.3%, p value 0.024 and 0.001, FDR 0.53 and 0.04). More details on other endpoints and other SNP will be presented, although in general no important association was found for other SNP mentioned.

Conclusions: Genetic variation in the MRP1 and UGT2B7 gene was highly associated with severe haematologic toxicity of FEC, while other previously described SNP were not validated. This is by far the largest breast cancer cohort in which the impact of genetic variability on toxicity was investigated.

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An Investigation of Interactions Between Genetic Variants and Established Risk Factors for Breast Cancer in the NCI Breast and Prostate Cancer Cohort Consortium (BPC3)

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Background: Recently various breast cancer susceptibility loci have been identified by genome wide association studies (GWAS). Relatively little is known about the possible interplay between these loci and established risk factors for breast cancer risk. Prospectively collected data from large populations are needed to test reliably for such gene-environment interactions.

Methods: We studied 8,576 women with breast cancer and 11,892 controls from the NCI Breast and Prostate Cancer Cohort Consortium (BPC3). We assessed whether 17 single nucleotide polymorphisms (SNPs) previously associated with breast cancer risk,
(*FGFR2*-rs2981582, *FGFR2*-rs3750817, *TNRC9*-rs3803662, 2q35-rs13387042, *MAP3K1*-rs889312, 8q24-rs13281615, *CASP8*-rs1045485, *LSP1*-rs3817189, *COL1A1*-rs2075555, *COX11*-rs6504950, *RNF146*-rs2180341, 6q25-rs2046210, *SLC4A7*-rs4973768, *NOTCH2*-rs11249433, 5p12-rs4415084, 5p12-rs10941679, *RAD51L1*-rs999737),
modified the odds ratios for established risk factors (age at menarche, parity, age at menopause, use of hormone replacement therapy, family history, height, body mass index, smoking status, and alcohol consumption). We also studied the possible differential effect of the polymorphisms by subgroups of tumor stage, estrogen receptor, progesterone receptor status and age at diagnosis.

Results: We confirmed the association of all but three SNPs (in *LSP1*, *COL1A1* and *RNF146*) with breast cancer risk. After correction for multiple testing, we did not find any significant interactions between SNPs and the established risk factors. We confirmed previously reported reports of differential effects of SNPs in *FGFR2* and *TNRC9* with estrogen and progesterone receptor status.

Conclusions: Our study provides evidence against the hypothesis that known common breast cancer loci strongly modify the associations