Background: The Eurocare-4 (2000–2002) period analysis documents a mean European age-adjusted 5-year relative breast cancer survival of 79% with higher individual figures for Finland (85.7%), Norway (84.1%) and Sweden (86.3%) (*Lancet Oncol 2007;8:784–96*). The corresponding mean figure for England was 77.8%. We now compare these predicted survival estimates with actual age-adjusted relative 5-year breast cancer overall survival for women diagnosed with invasive breast cancer in the East of England from 2000 to 2002.

Method: The East of England covers a population of 5.5 million people. Five-year age-adjusted relative breast cancer survival was calculated overall, and in specific age groups, for 10,787 women with invasive breast cancer diagnosed from 2000 to 2002 in the East of England for comparison with the results from the Eurocare-4 study.

Results:

Age-adjusted 5-year relative breast cancer survival in East of England for period 2000–2002.

Age group	Number of patients	Relative survival	95% CI
45–54	2563	87.5%	86.1–88.9
55–64	2945	89.5%	88.1–90.9
65–74	2335	83.9%	81.8–86.1
75+	2944	73.3%	70.1–76.4
All women	10,787	82.5%	81.4–83.6

Conclusion: These data confirm breast cancer survival rates for East of England that are close to European best figures for women aged 45–64. The mean survival of 82.5% for all women however is being reduced by worse survival in women aged 65+ and a strategy that ensures optimal breast cancer treatment for women in this age group should allow the mean survival to improve even further.

doi:10.1016/j.ejcsup.2010.06.053

O-53 A STUDY OF THE VALUE OF COMPREHENSIVE GERIATRIC ASSESSMENT (CGA) IN OLDER WOMEN WITH PRIMARY BREAST CANCER – PRELIMINARY RESULTS

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Background: Despite being an important health issue, breast cancer in older women is under-researched. This study aimed to identify how CGA may be linked to treatment decision making.

Methods: Women ⩾70 years with newly diagnosed primary breast cancer in Nottingham were invited to take part. Decision for a particular treatment was made between the clinical team and the patient, and this was not part of the study. Each patient then completed an established CGA tool – a multi-dimensional questionnaire incorporating information on demographics, mood, social activities and support, medication, functional status, cognition, nutritional state and co-morbidities.

The study is ongoing. At this preliminary analysis, 20 patients (aged 70–87) were recruited from different treatment groups (mastectomy $n = 8$, breast conserving surgery, $n = 4$, primary endocrine therapy (PET) $n = 7$, primary radiotherapy $n = 1$).

Results: Compared to patients undergoing surgery, the PET group was found to be older (median age 85 versus 76). Patients on PET also reported having lower median physical functioning (7.5 versus 11.5) and social support (66.67 versus 89.95) scores, mood levels (67.65 versus 85.29) and more co-morbidities (median 4 versus 2).

Conclusions: Using a CGA tool may be beneficial in guiding treatment decision. This ongoing study may establish a tool specific to the context of older women with primary breast cancer. This could then become part of routine consultation and may help identify patients who would require input of a geriatrician. When combined with quality of life measures and biological information, there is potential to provide a holistic approach to this under-served population.

doi:10.1016/j.ejcsup.2010.06.054

O-54 INVOLVEMENT OF MiR-34A IN RESISTANCE OF BREAST CANCER CELLS TO DOCETAXEL

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Introduction: Understanding the mechanisms of drug resistance is important to improve and deliver effective therapy. MicroRNAs (miRNA) are small RNA molecules that regulate gene expression, hence we hypothesised that gene silencing, by altered miRNA expression, causes docetaxel resistance.

Methods: Quantitative PCR-based miRNA arrays were used to examine the role of miRNAs in acquired resistance of breast cancer cells (MCF-7 and MDA-MB-231) to docetaxel. Quantitative PCR and western analysis were used to measure target gene mRNA and protein expression, respectively. MicroRNA expression was modulated and docetaxel response was measured by cell viability assay.

Results: We found 299 and 226 miRNAs altered in MCF-7 and MDA-MB-231 docetaxel-resistant cells, respectively. Only miRNA alterations that reached statistical significance, which targeted experimentally validated genes involved in cell cycle, apoptosis or drug resistance, were selected for further investigation. Docetaxel resistance was associated with increased expression of miR-34a and miR-141 and decreased expression of miR-7, miR-16, miR-30a, miR-125a-5p, miR-126 and miR-429. Computational target prediction revealed 11 candidate genes targeted by these miRNAs. Quantitative PCR and western analysis confirmed decreased expression of only two genes, BCL2 and cyclinD1, in docetaxel-resistant cells, which are both targeted by miR-34a. Inhibition of miR-34a enhanced response to docetaxel in MCF-7 docetaxel-resistant cells whereas overexpression of miR-34a conferred resistance in MCF-7 docetaxel-sensitive cells. Modulation of miR-34a expression was correlated with expected BCL2 and cyclinD1 protein expression changes.

Conclusions: Our findings suggest that miR-34a is involved in docetaxel resistance, which may act by targeting BCL2 and cyclinD1.

doi:10.1016/j.ejcsup.2010.06.055

O-55 TRANSLATIONAL LANDSCAPE OF EPITHELIAL MESENCHYMAL TRANSITION IN MOLECULAR CLASSES OF INVASIVE BREAST CANCER

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Epithelial Mesenchymal Transition (EMT), as defined by loss of epithelial characteristics and gaining a more mesenchymal-like phenotype, has been largely reported *in vivo*. However, the actual occurrence of events defining EMT is rarely fully observed *in vivo*. We aimed to explore the translational landscapes of EMT in breast cancer (BC) with relevance to potential triggering pathways and BC molecular subtypes. Clustering analysis was performed on a well-defined clinically annotated series of invasive non-lobular BC ($n = 431$) prepared as tissue microarray (TMAs). A large panel of biomarkers including cadherins, TGFβ1, PIK3CA, pAkt, cytokeratins, Erb-family members and hormone receptors, has been studied. Differential expression of EMT markers was observed between molecular BC subtypes (Luminal1 and 2, $HER2^+$, and basal-like (BLBC), where BLBC expressed lower E-cad, higher P-cad, smooth muscle actin and PIK3CA, relative to $HER2^+$ BC that expressed highest levels of N-cad, TGFβ1 and PIK3CA. Within luminal tumours subdivisions, expression levels of N-cad, TGFβ1, pAkt and PIK3CA differed considerably. N-cad contributed to cluster separation more than E-cad ($F = 13.14$ and 1.68, respectively). Moreover, E-cad/N-cad switch occurred more frequently in BLBC and $HER2^+$. Significant differences were observed between these four clusters for breast cancer-specific and disease-free survivals ($p < 0.001$).

BLBC and $HER2^+$ BC preferentially displayed EMT/cadherin switch than luminal BC, explaining their indigenous tendency for progression. In addition, EMT/cadherin switch programs in BC appear to occur synergistically with TGFβ1 and PIK3/Akt pathways activation. These data explain, at translational level, the varied clinical behaviour of BC molecular classes, thus could help developing targeted therapies against EMT-associated pathways.

doi:10.1016/j.ejcsup.2010.06.056

O-56 HIGH EXPRESSION OF SPHINGOSINE 1-PHOSPHATE RECEPTORS, $S1P_1$ AND $S1P_3$, SPHINGOSINE KINASE 1 AND ERK-1/2 IS ASSOCIATED WITH DEVELOPMENT OF TAMOXIFEN RESISTANCE IN ER POSITIVE BREAST CANCER PATIENTS

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Cell line studies demonstrate that sphingosine kinase 1 (SK1) and extracellular signal regulated kinase 1/2 (ERK-1/2) interact in an oestrogen receptor (ER) dependent manner to influence breast cancer cell growth and migration. A cohort of 304 ER positive breast cancer patients, were utilised to investigate the prognostic significance of SK1, sphingosine 1-phosphate receptors 1, 2 and 3 ($S1P_1$, $S1P_2$ an $S1P_3$) and ERK-1/2 expression. Expression levels of SK1, $S1P_1$, $S1P_2$ and $S1P_3$ were established by immunohistochemistry. Cytoplasmic and nuclear SK1 expression was associated with shorter time to recurrence on tamoxifen (recurrence time) ($p = 0.022$ and $p = 0.016$, respectively) and high membrane $S1P_1$ expression was also associated with shorter time to recurrence ($p = 0.008$). High cytoplasmic $S1P_1$ and $S1P_3$ expression were associated with shorter disease specific survival ($p = 0.036$ and $p = 0.019$). Those patients with tumours that expressed high levels of both cytoplasmic SK1 and ERK-1/2 had significantly shorter recurrence time than those that expressed low levels of cytoplasmic SK1 and cytoplasmic ERK-1/2 ($p = 0.00008$), with a difference in recurrence time of 10.5 years. Similarly, high cytoplasmic $S1P_1$ and cytoplasmic ERK-1/2 expression ($p = 0.004$) and high cytoplasmic $S1P_3$ expression and cytoplasmic ERK-1/2 expression ($p = 0.004$), were associated with shorter recurrence time. These results support a model in which the interaction between SK1, $S1P_1$ and/or $S1P_3$ and ERK-1/2 might drive breast cancer progression and this therefore warrants further investigation.

doi:10.1016/j.ejcsup.2010.06.057

O-57 SCREEN DETECTED DCIS IN THE EAST MIDLANDS REGION: COMPARISONS IN TREATMENT AND OUTCOME OVER TIME (1988–2003)

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A retrospective study was carried out comparing three cohorts of consecutive patients diagnosed with DCIS via the NHSBSP in the East Midlands region. Diagnostic, treatment and follow-up outcome data was collected by individual patient case notes review, and where necessary by contacting general practitioners. Kaplan–Meier survival analysis was performed using SPSS.

Histological excision margins were increasingly clear over time 88% (88/93), 91.5% (94/97) and 98% (00/03). The overall local recurrence free survival rate was identical for both earlier periods with 92% at 5 years but improved to 96.1% over 2000/03. 40–56% of all local recurrences were invasive; 13/23 (88/93), 14/26 (94/97), and 8/21 (00/03). Use of tamoxifen within the three cohorts was similar (44–46%) and made no significant difference to rates of local or contralateral recurrence free survival. Significant differences in local recurrence rates by operation type were observed (see Table 1).

Conclusion: Local recurrence rates after breast conserving surgery for screen detected DCIS have reduced over time. This is likely to be related to higher rates of non-operative diagnosis, combined with improved histological assessment (grading and