Imperial College Healthcare NHS Trust, Charing Cross, UK. [f] *St. Mary's Hospital, Imperial College Healthcare NHS Trust, London, UK.* [g] *Edinburgh Cancer Centre, Edinburgh, UK*

Background: Trastuzumab was licensed for adjuvant therapy in early breast cancer (EBC) in the UK in 2006. The objectives of this multicentre audit were to determine the incidence of HER2+ breast cancers, proportion of HER2+ EBC women who received Trastuzumab and ascertain reasons why some HER2+ patients did not receive Trastuzumab.

Methods: Data collected for all invasive breast cancers diagnosed at seven UK centres over 18-months from 2007 onwards. All HER2+ cancers diagnosed by a combination of IHC and FISH identified using each centre's database. Case records checked and reasons noted if they had not received Trastuzumab.

Results: Patients (4488) diagnosed with invasive breast cancer. 645 (14%) were HER2+ cancers, 523 being EBCs. 326 (62%) HER2+ EBCs received Trastuzumab.

Reasons for not receiving Trastuzumab	*n* = 197(%)
Tumour ⩽10 mm, node negative	65(33)
Small node negative tumours (11–20 mm)	18(9)
Age	42(21)
Comorbidities	27(13)
Therapy refused	28(14)
Other reasons	17(9)

Conclusions: Incidence of HER2+ breast cancers is 14%, majority being EBCs (81%). Only 62% of the HER2+ EBC patients received Trastuzumab. Whilst the commonest reason for not receiving Trastuzumab is small node negative tumours (which is compatible with UK guidelines), an equal number of patients potentially missed optimal therapy for reasons not noted in the guidelines. Recent studies have demonstrated that being HER2+ is a significant risk factor for relapse in patients previously perceived to be at low risk and no HER2+ patient should now be considered low risk.[1]

Reference:

1. Tovey SM et al. Poor survival outcomes in HER2+ breast cancer patients with low-grade, node-negative tumours. *BJC* 2009;**100**(5):680–3.

doi:10.1016/j.ejcsup.2010.06.040

O-40 BREAST CANCER TREATMENT IN THE ELDERLY

I. Monypenny [a], J. Sidhu [a], C. Lagord [b], O. Kearins [b], S. Cheung [b], G. Lawrence [b]. [a] *University Hospital of Wales, Cardiff, UK.* [b] *West Midlands Cancer Intelligence Unit, Birmingham, UK*

Objective: Of the 49,452 breast cancers diagnosed in the UK in 2006, 25,049 (51%) were diagnosed symptomatically in patients aged 50 and over. This study compares the nature and treatment of symptomatic invasive cancers in patients aged 50–69 and 70 years or over ('elderly').

Methods: Data were extracted from national audit databases and from the merged cancer registry database linked to HES.

Results: 84% of Patients aged 50–69 had surgery recorded compared with 55% of patients aged 70 or over. Surgery rates increased to 79% in 'elderly' patients known to be ER negative. 'Elderly' patients were more likely to have a mastectomy (61% versus 50%). For surgically treated tumours, prognostic factors were similar in both groups: node positivity: 54% in 50–69 versus 50% in 'elderly', ER status (73% ER positive in 50–69 versus 77% in 'elderly') and grade (52% Grade 1 or 2 in 50–69 versus 59% in 'elderly'). For cases with adjuvant therapy data available, radiotherapy after conserving surgery was slightly lower in the 'elderly' (87% versus 94%), chemotherapy for node positive patients was much lower in the 'elderly' (21% versus 75%) and more 'elderly' patients received hormone therapy (90% versus 83%).

Conclusion: 'Elderly' patients were less likely to receive surgery or chemotherapy. Patient choice, the presence of co-morbidities, lack of evidence on the relative risks/benefits of adjuvant therapy or reduced access to surgery for older patients are factors which might explain the differential treatment of these patients.

doi:10.1016/j.ejcsup.2010.06.041

O-41 AGE SPECIFIC BREAST CANCER RELATIVE SURVIVAL IN THE EAST OF ENGLAND

Alaa M.G. Ali [a], Gordon Wishart [b], David Greenberg [c], Paul Pharoah [a,d]. [a] *Department of Public Health and Primary Care, Cambridge, UK.* [b] *Cambridge Breast Unit, Addenbrooke's Hospital, Cambridge, UK.* [c] *Eastern Cancer Registration and Information Centre, Cambridge, UK.* [d] *Department of Oncology, University of Cambridge, Cambridge, UK*

Background: Breast cancer relative survival (BCRS) tends to be poorer in older women, but the reasons for this are not clear. We examined the influence of patient and tumour characteristics, and treatment on BCRS to see if these could explain the age specific effects.

Methodology: Data for 14,048 female breast cancer patients diagnosed from 1999 to 2007 aged 50 years or over were obtained from the Eastern Cancer Registration and Information Centre. We estimated relative 5- and 10-year survival for patients in four age groups (50–69, 70–74, 75–79, and 80+). We also modelled relative excess mortality rate (REM) adjusting for potential confounders. Covariates included in the analysis were age, TNM stage, histologic grade, ER status, mode of detection, volume at hospital of diagnosis, and treatment (surgery, radiotherapy, chemotherapy and hormonal therapy.

Results: Median follow-up time was 4.7 years. Relative 5-year survival was 90%, 81%, 76% and 68% for patients aged 50–69, 70–74, 75–79 and 80+, respectively. Corresponding relative 10-year survival was 84%, 77%, 66% and 60%. Similar patterns were seen for both ER+ and ER− and for low and high volume hospitals.

Unadjusted REM was 1.95, 2.86 and 4.30 for patients aged 70–74, 75–79 and 80+, respectively (50–69 reference). These were

attenuated after adjusting for confounders (REM – 1.50, 1.38 and 1.27).

Conclusion: We confirmed poorer BCRS in older women in our region. This was partially explained by known prognostic factors. Further research is needed to determine whether biological differences or sub-optimal management can explain the residual excess mortality.

doi:10.1016/j.ejcsup.2010.06.042

O-42 EARLY OPERABLE PRIMARY BREAST CANCER IN OLDER (⩾70 YEARS) WOMEN (EPCS) – BIOLOGY AND CLINICAL SIGNIFICANCE

B.M. Syed [a], W. Al-khyatt [a], A.R. Green [b], E.C. Paish [b], D.A.L. Morgan [c], I.O. Ellis [b], K.L. Cheung [a]. [a] *Division of Breast Surgery, Nottingham University Hospitals, Nottingham, UK.* [b] *Division of Pathology, University of Nottingham, Nottingham University Hospitals, Nottingham, UK.* [c] *Department of Oncology, Nottingham University Hospitals, Nottingham, UK*

Introduction: Biology of breast cancer appears to change with age. Most studies are small/from multiple centres limiting their importance.

Methods: From 1973 to 2009, 2000+ EPCs were managed in Nottingham. Oestrogen receptor (ER) was assessed by immunohistochemistry (giving an H-score) on core biopsy for all patients. A total of 831 patients had primary surgery and 575 had good quality tumour samples available for tissue microarray analysis.

Results: Comparing these 831 patients with a younger (<70 years) series ($N = 1809$), expression of ER ($p < 0.001$), p53, HER4, CK14, bcl2 ($p < 0.000$) and CK 17 ($p < 0.05$) was found to increase with age, while reverse was seen with CK 7/8 ($p < 0.002$), ki67 and E-Cadherin ($p < 0.000$). No change was observed in PR, HER2, CK5/6, CK19 and MUC1 expression.

At 66-month median follow-up, for those who did not receive adjuvant systemic therapy ($N = 306$), tumour size ($p < 0.042$), grade ($p < 0.046$), axillary stage ($p < 0.000$) and PR ($p < 0.017$) were found to be independent prognostic factors.

At 49-month median follow-up, for patients with ER+ (H-score ⩾ 50) tumours, those with H-score ⩾ 250 had equivalent 5-year breast cancer specific survival (BCSS) regardless of primary treatment (surgery vs primary endocrine therapy (PET) 95% versus 93%, $p = 0.715$). For patients on PET, all those with H-score ⩾ 250 achieved clinical benefit as compared to 11 patients with H-score < 250 who progressed, at 6 months ($p < 0.03$), the former also had better BCSS ($p < 0.01$).

Conclusion: The pattern suggests a less aggressive tumour phenotype with advancing age. The ER H-score appears as an excellent surrogate for clinical outcome for ER+ EPCs. It is available at diagnosis and has a great value in guiding discussion of therapeutic options.

doi:10.1016/j.ejcsup.2010.06.043

O-43 A KRAS MICRORNA BINDING SITE VARIANT IS A GENETIC MARKER OF RISK FOR TRIPLE NEGATIVE BREAST CANCER

H.M. Heneghan [a], N. Miller [a], T. Paranjape [c], F.J. Slack [b], J.B. Weidhaas [c], M.J. Kerin [a]. [a] *Department of Surgery, National University of Ireland, Galway, Ireland.* [b] *Department of Molecular, Cellular and Developmental Biology, Yale University, USA.* [c] *Department of Therapeutic Radiology, Yale University, USA*

Introduction: MiRNAs exert their regulatory effect on gene expression by binding to the 3′ untranslated region (UTR) of target mRNAs. The let-7 miRNA family are global genetic regulators critically important for controlling oncogene expression (e.g. *KRAS*). Dysregulated let-7 expression is associated with many malignancies including breast cancer, and it is hypothesized that defective interaction between let-7 and its target *KRAS* underpins this association and oncogenesis. We hypothesized that a single nucleotide polymorphism (SNP) in the *let-7*-binding site in *KRAS* disrupts *let-7* regulation of the oncogene and thus predisposes to breast cancer.

Methods: A population analysis of the association of the *KRAS* variant and breast cancer was performed on a cohort of 1010 breast cancer patients and 1497 age-matched healthy controls. Genomic DNA isolated from all participants was amplified using PCR assays designed specifically to identify the T (wild type) or G (variant) allele. Genotyping results were correlated with patients' clinicopathological parameters.

Results: The *KRAS* variant was present in 15% of all breast cancer patients, compared with baseline prevalence of <7%. In particular the *KRAS*-variant predicted a significantly increased risk of developing triple negative breast cancer in premenopausal women (OR = 4.78, CI = 1.71–13.38, $p = 0.015$), and patients with the variant allele were significantly more likely to present with advanced stage disease ($p = 0.03$).

Conclusion: These seminal findings suggest that the *KRAS*-variant acts as a genetic marker of risk for developing triple negative breast cancer. Predicting risk for this subtype is critically important, to permit early screening and intervention for 'at-risk' individuals.

doi:10.1016/j.ejcsup.2010.06.044

O-44 GENE–ENVIRONMENT INTERACTIONS IN 7610 WOMEN WITH BREAST CANCER: PROSPECTIVE EVIDENCE FROM THE MILLION WOMEN STUDY

Ruth C. Travis, Gillian K. Reeves, Jane Green, Diana Bull, Sarah J. Tipper, Krys Baker, Valerie Beral, Richard Peto, John Bell, Diana Zelenika, Mark Lathrop, for the Million Women Study Collaborators. *Cancer Epidemiology Unit, University of Oxford, UK*

Background: Genome-wide association studies, together with analyses of specific candidate polymorphisms, have identified a number of low-penetrance breast cancer susceptibility loci. Information is scarce about the combined effects on breast cancer incidence of these genetic variants and of environmental factors (reproductive, behavioural, and anthropometric risk factors for