

these cases underwent a mastectomy; whereas the overall mastectomy rate was 50%.

Analysis of the cases collated by the BCCOM project in years 1–3 will be undertaken to evaluate data quality and performance. Delegates at the conference will be invited to comment on the measures developed, and the use of these measures as possible surrogates for patients' clinical outcomes will be discussed.

#### **O-7** Micro-RNA expression profiling in primary breast tumours

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**Introduction:** The role of micro-RNAs in the regulation of proliferation, differentiation and apoptosis has advocated them as a novel molecular mechanism in the aetiology of carcinogenesis. MicroRNA expression has been shown to be dysregulated in a number of human cancers, including breast cancer.

**Aims:** To identify microRNAs that are aberrantly expressed in breast tumour tissue and examine correlations with established clinicopathological variables.

**Methods:** Whole genome microRNA profiling was performed in six early stage breast cancer specimens. Expression of selected differentially expressed microRNAs was validated using RQ-PCR in a larger cohort of 54 breast tumours, 5 benign, and 5 normal breast tissues. Associations between relative expression of specific microRNAs, established clinicopathological variables and hormone receptor status were examined.

**Results:** 53 of 452 microRNAs were differentially expressed across the six tumour samples. Specific microRNAs which were validated in the larger cohort of samples using RT-Q-PCR included *miR-21*, *miR-195*, *miR-10b* and *miR-154\**. Tumour samples exhibited higher *miR-21* expression than normal breast tissue. Conversely, *miR-10b* and *miR-195* were consistently expressed at lower levels in tumour versus benign and normal breast tissue. *miR-195* and *miR-154\** expression was significantly lower in oestrogen receptor positive (ER) than ER negative tumours. ( $p=0.005$ ,  $p=0.001$ ). Expression was independent of other clinicopathological variables.

**Conclusions:** The increased expression of *miR21* and decreased expression of *miR-10b* and *miR-195* in tumor tissues implicates these miRNAs in oncogenesis and tumour suppression respectively. We have shown that *miR-195* and *miR-154\** are differentially expressed in breast tumours according to ER status, highlighting their importance in specific breast cancer phenotypes.

#### **O-8** Factors predicting survival after neoadjuvant therapy with aromatase inhibitors

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**Background:** Few studies have investigated factors predicting outcome following neoadjuvant endocrine therapy. This study aimed to determine factors predicting survival after neoadjuvant treatment with aromatase inhibitors (AI's).

**Methods:** 153 postmenopausal women with large/locally advanced estrogen receptor rich tumours (ER 5–8) were treated for 3 months with letrozole, anastrozole or, exemestane. The mean patient age was 74.7 years. Tumour biopsies were obtained prior to starting therapy and at 3 months. At 3 months patients underwent surgery with nodal assessment or, continued AI therapy. Responding patients continued AI therapy post-operatively. Median

follow up was 41 months. Five year survival was 63.1% and cause specific survival (CSS) 79.8%.

**Results:** At 3 months only 3% had progressive disease and 67 had responded (>50% reduction in volume). In the univariate analysis T stage ( $p=0.03$ ), surgical node status ( $p=0.0005$ ), Ki67 at diagnosis ( $p=0.036$ ), 3 month % reduction in Ki67 ( $p=0.0027$ ) and 3 month Ki67 ( $p=0.03$ ) were significantly correlated with CSS. In the proportional hazards analysis significant variables were number of positive nodes ( $p=0.0007$ ), % reduction in Ki67 ( $p=0.0029$ ) and, tumour grade ( $p=0.0383$ ). Excluding those available at diagnosis significant variables were baseline Ki67 ( $p=0.02$ ) and T stage ( $p=0.02$ ).

**Conclusion:** In post-menopausal women treated with neoadjuvant AI therapy: (i) Two thirds with ER rich large/locally advanced breast cancers responded to 3 months of treatment and, (ii) Surgical node status, % reduction in Ki67 and, tumour grade predicted death from breast cancer.

#### **O-9** ONCOPOOL – A European Database in 16,893 cases of breast cancer: comparison with SEER

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11 European Breast Units from 10 countries retrospectively entered consecutive cases diagnosed in each unit in periods between 1990–99. Cases were women, age  $\leq 70$  with primary tumours <5 cm diameter. Data on diagnosis, surgical and adjuvant treatments, pathology and biology, recurrences and survival.

- Factors at diagnosis
  - Tumour size: 21%  $\leq 1$  cm, 28%  $\leq 2$ , 29%  $\leq 3$ , 10%  $\leq 4.9$
  - LN status: LN neg 66%, LN 1–3+ 24%, LN 3+ 10%
  - Grade: I 29%, II 42%, III 29%
- Second order polynomial curves demonstrate the relations of the three LN stages with tumour size and between grade and stage
- Overall survival was 91% 5 yr, 81% 10 yr and 78% 14 yr (Life table)
- The survival data provides validation of the updated prognosis according to the Nottingham Prognostic Index (to be separately presented).

The US SEER (Surveillance, Epidemiology and End Results) Database has long been regarded as giving the standards in Primary Breast Cancer for distribution of pathological factors and prognoses. There was a great amount of incomplete data.

Comparison of the SEER estimates of prognosis according to TNM are shown in ONCOPOOL to be greatly inferior to other means of estimation (Table).

	TNM Predicted	NPI Predicted		ONCOPOOL	
	10 yr % OS	Grade	NPI Group	10 yr % BCS	Observed 10 yr % BCS
$\leq 2$ cm, LN –	94	I	EPG	96	94
$\leq 2$ cm, LN –	94	III	MPG I	81	94
$\leq 2.5$ cm, LN –	88	I	GPG I	93	93
$\leq 2.5$ cm, LN –	88	III	MPG II	74	76
$\leq 2.5$ cm, LN –	76	I	MPG I	81	84
$\leq 2$ cm, LN –	76	III	PPG	55	53
$\leq 2$ cm, LN –	58	I	MPG II	74	76
$\leq 2.5$ cm, LN –	58	III	PPG	55	53