We have assessed HER2 status in a large well-characterised breast cancer series prepared as tissue microarray ($n = 1858$) using IHC (HercepTest, DakoCytomation) and chromogenic ISH (CISH; DuoCISH, DakoCytomation) in order to identify relationships with clinico-pathological variables and patient outcome. None of these cases have received anti-HER2 therapy.

There was excellent overall concordance between HercepTest negative (scores 0/1+) and positive (3+) with CISH positive/negative (defined as HER2/Chr17 copy number ratio of $\geqslant 2$; $p < 0.001$). Twelve percent of cases were identified as HER2 positive (those with 3+ HercepTest scores or 2+ with gene amplification). Of the 74 borderline HercepTest 2+ cases, 44 cases (59%) showed HER2 gene amplification. We identified that HercepTest 2+ non-amplified cases were not significantly different from those amplified 2+ or 3+ cases with respect to their clinical outcome (BCSS and DFS).

The overall concordance between HercepTest and CISH analysis for HER2 status was excellent. All HercepTest 2+ cases identified were observed to have poor outcomes similar to those HercepTest 3+ cases regardless of gene amplification status. In the current clinical environment, cases exhibiting IHC 2+ with non-amplified HER2 gene status are not offered targeted HER2 therapy but do exhibit aggressive clinical behavioural characteristics and therefore optimal treatment strategies for these patients need to be determined.

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O-18 PARP1 EXPRESSION IN HORMONE ESTROGEN RECEPTOR NEGATIVE BREAST CANCER: PREFERENTIAL EXPRESSION IN BASAL-LIKE AND HER2-POSITIVE TUMOURS

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Nuclear poly (ADP-ribose) polymerases (PARPs) are a family of global monitor of chromatin structure and DNA damage repair. The relative expression levels of PARP1 protein in estrogen receptor negative (ER–ve) BC remain unclear. Therefore the aim of this study was to investigate PARP1 protein expression in ER–ve BC with relevance to molecular subtypes and disease outcome.

Methods: PARP1 protein expression was assessed, using immunohistochemistry, in a well-characterised series of ER–ve primary operable invasive BC cases ($n = 251$) with long term clinical follow-up. Results were correlated with molecular and clinicopathological parameters and patients' outcome.

Results: PARP1 nuclear expression was classified as high or low using a cut-off of 80 H-score, determined using X-Tile bio-informatics software. One hundred and thirty five (53.8%) of the informative cases were classified showing high expression. Significant positive correlation was found between PARP1 expression and BRCA1 expression ($p = 0.002$) but no association was found with p53. High PARP1 expression was observed in both basal-like (HER2– and CK5/6 and or EGFR+) (60%) and HER2+ (64%) compared with triple negative (TN) non-basal BC classes (45%). PARP1 expression was significantly associated with BC specific survival ($p = 0.01$). When analysis was assessed by the molecular subtype, the association of PARP1 expression with improved survival was restricted to TN tumours.

Conclusion: We have observed a positive correlation between PARP1 protein expression and BRCA1 expression. Although high PARP1 expression is seen in ER–/HER+ and HER– tumours, its association with survival was only found in the ER–/HER2– subtype. Thus, its targeted inhibition may particularly benefit patients with TN BC.

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O-19 COMPARISON OF IMPUTATION METHODS FOR MISSING IMMUNOHISTOCHEMICAL MARKERS IN A STUDY OF BREAST CANCER PROGNOSIS

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Background: Tissue micro-arrays (TMA) are increasingly used to generate data for studies of tumour molecular phenotype however, TMA data are particularly prone to missingness. A variety of methods to deal with missing data are available; these have been extensively evaluated using simulated data, but there has been no empirical evaluations of these methods using real TMA data.

Methods: We pooled data from over 11,000 cases of invasive breast cancer from five studies that collected information on seven prognostic indicators including four molecular markers, together with survival time data. We compared the results of a multi-variate Cox regression using complete case analysis (CCA), mean substitution (MS) and multiple imputation (MI). We also performed an analysis in which missing data were simulated under different assumptions.

Results: Over half the cases had data on at least one of the seven variables and 10.5% had missing data on 4 or more. The hazard ratio estimates based on multiple imputation and mean substitution, were similar with similar standard errors. Hazard ratio estimates and confidence intervals (Table). The results from CCA were less precise (wider confidence limits). Accuracy of the estimates was based on the simulated data with CCA having the least accurate results.

Hazard ratios and confidence intervals using mean substitution and multiple imputation.

Method	ER status	PR status	HER2 status	BCL2 status
Multiple imputation – HR (CIs)	0.43 (.35–54)	0.39 (.30–.50)	1.25 (1.13–1.40)	0.85 (.76–.96)
Mean substitution – HR (CIs)	0.40 (.32–.49)	0.37 (.29–.46)	1.31 (1.17–1.46)	0.82 (.74–.92)