ALCAM protein expression. A modified H-score system was used to enumerate the intensity and proportion of cytoplasmic and membranous staining in the neoplastic component, using a number of tumour stratification approaches. Univariate and multivariate analysis was used to examine the association between ALCAM expression and clinicopathological parameters.
Results: ALCAM under-expression was significantly related to increased histological grade ($p = 0.010$) and distant metastases ($p = 0.035$) but not recurrence ($p = 0.995$). ALCAM under-expression was associated with significantly worse overall survival ($p = 0.022$) and an odds ratio of 0.56 compared to 2.12 for the Nottingham Prognostic Index (NPI).
Conclusion: Loss of the cell adhesion molecule ALCAM is a significant predictor of poor survival in breast cancer. A possible explanation for this observation is enhancement of metastatic tumour spread resulting from the loss of cell-to-cell adhesion affected by ALCAM.

O-94 Stat3 expression is a poor prognostic marker for invasive breast cancer

H. Cain*, S. Amonkar, A. Davison, E. Scott, C. Hodgson, D. Hemming, B.K. Shenton, W. Cunliffe, T.W.J. Lennard, D.A. Browell. *Queen Elizabeth Hospital and University of Newcastle upon Tyne, UK*

Introduction: Signal Transducer and Activator of Transcription 3 (STAT3) is a cell cycle regulatory transcription factor over-expressed by some breast cancers. STAT3 activation contributes to cell survival and resistance to apoptosis and radiation treatment due to its relation with the expression of survivin and Bcl-2. Inhibition of its action results in apoptosis and radio sensitisation of breast cancer cells. The aim of this study is to determine if the expression of STAT3 is a significant prognostic marker in invasive breast cancer.
Methods: Consecutive patients with invasive breast cancer undergoing surgical excision during a 12 month period were selected. STAT3 expression was assessed using a novel immunohistochemistry (IHC) technique on paraffin embedded samples and follow up data of the cohort was recorded.
Results: Of the 205 cases assessed, 151 cases were STAT3 negative and 54 cases expressed STAT3. STAT3 expression was associated with node positive disease ($p \leqslant 0.001$), ER negative tumours ($p \leqslant 0.01$), a high NPI ($p \leqslant 0.001$) but not with HER2 expression ($p \geqslant 1.0$). The 5yr survival was poorer in STAT3 positive patients compared to STAT3 negative patients (72.3% c.f. 85.3%) ($p = 0.04$). The co-expression of STAT3 and HER2 decreased 5yr survival by 16.5% compared to HER2 positive STAT3 negative patients (see table 1).

Table 1. Co-expression of HER2 and STAT3 and 5 yr survival

	HER2 Negative	HER2 Positive
STAT3 Negative	88.1%	76.5%
STAT3 Positive	80.6%	60%

Conclusion: The elevated expression of active STAT3 is a marker of poor disease outcome and should now be considered as a prognostic marker. The STAT3 status of HER2 positive breast cancers and its implication for survival is an important finding.

O-95 TOPO II is an independent predictor of survival in unselected breast cancer

A. Pancholi*, D.G. Powe, R.M. Ganesh, M. Lambros, J.S. Reis-Filho, E. Rakha, I.O. Ellis. *Nottingham University Hospitals, University of Nottingham and Institute of Cancer Research, London, UK*

Introduction: The identification of new biomarkers is contributing to improvements in the predicting the response to treatment in breast cancer. Topoisomerase II alpha (*TOP2A*) is involved in the relaxation of DNA during replication and transcription. Several studies suggest that amplification of the *TOP2A* gene associates with response to anthracycline-based chemotherapy, however few studies have analysed the prognostic impact of TOP2A in a population based cohort of breast cancer patients.
Aim: To assess *TOP2A* as a predictor of survival in patients with breast cancer, comparing fluorescent (FISH) and chromogenic (CISH) in situ hybridisation techniques in high throughput tissue microarrays (TMA).
Materials and Methods: Tissue microarray (TMA) sections containing 183 and 269 well-characterised unselected breast tumours were subjected to fluorescent (FISH) and digoxigenin (CISH)-labelled *TOP2A* in situ hybridisation, respectively. *TOP2A* amplification was defined by 50% or greater of at least 30 neoplastic nuclei showing 5 or more signals in the CISH-treated sections, or by a ratio of >2 for cancer cells probed by FISH, compared to a chr17 centromeric probe. Uni- and multivariate analysis was used to test for association between *TOP2A* and clinical parameters.
Results: FISH and CISH showed excellent agreement ($p = 0.0001$), with 20 and 25 tumours showing amplification by *TOP2A* FISH and CISH, respectively. *TOP2A* amplification associated with high tumour grade (>0.05), metastases (>0.03), recurrence ($p > 0.015$), disease-free interval ($p = 0.002$), and overall survival (OR = 2.69).
Conclusion: *TOP2A* is an independent predictor of survival, equalling or bettering the Nottingham Prognostic Index. *TOP2A* gene status assessment by FISH and CISH techniques show excellent correlation.

O-96 Accelerated E-CMF (accE-CMF) chemotherapy with pegfilgrastim support in early stage breast cancer is associated with low incidence of severe lymphopenia

N. Singh, S.J. Bowden, L. Gross, S. Anwar, C.J. Poole, D. Rea*. *University Hospitals Birmingham and University of Birmingham, UK*

Background: Accelerated chemotherapy, doxorubicin-cyclophosphamide followed by paclitaxel (accAC-P), with GCSF support, has been associated with high incidence of grade 3 or 4 lymphopenia (>60% patients), possibly contributing to a risk of pnemocystis carinii pneumonia (Tolaney SABCS 2006). We have recently conducted a study to explore the feasibility of accelerating E-CMF, reporting dose intensity and toxicity data (Rea ASCO 2007).
Methods: Patients with early breast cancer were treated with two chemotherapy schedules. Schedule A comprised epirubicin 100 mg/m2 repeated every 14 days (d) with pegfilgratim (P) on day 2 for 4 cycles followed by CMF 600/40/600 mg/m^2 day 1&8 with P on day 9 repeated every 21d for 4 cycles. Schedule B had the same epirubicin schedule followed by six cycles of CMF 800/50/600 mg/m^2 with P on day 2 repeated every 14d. FBC were recorded every 7d. We analysed lymphocyte data from 2 centres, 21 patients had schedule A and 19 schedule B. We also examined day 1 lymphocyte counts from 40 patients treated with conventional E-CMF.