chemotherapy (n = 31), whereas no significant impact was seen in node-positive patients treated either by CMF chemotherapy (n = 49) (DFS: p = 0.605; OS: p = 0.934) or by adjuvant endocrine therapy (tamoxifen) alone (n = 106) (DFS: p = 0.735; OS: p = 0.275). While median DFS and OS in anthracycline-treated patients was >10 years if tumours showed high EFEMP1 expression, it was only 3.1 years (DFS) respectively 4.5 years (OS) in cases with low EFEMP1 expression.

Conclusions: The results point to a predictive value of EFEMP1 expression regarding anthracycline response in node positive patients, which needs to be further validated in larger collectives of homogeneously treated breast cancer patients. In view of clinically emerging angiogenesis inhibitors, identification and characterization of components of the angiogenic pathway as specific prognostic as well as predictive markers is of great relevance for the success of this treatment option. EFEMP1, with its anti-angiogenic properties, may serve here as an important molecular marker for defining an adequate tumour-biology oriented therapeutic strategy.

33 Poster Discussion

AlphaB-crystallin predicts poor breast cancer survival in basal-like tumors

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Background: Basal-like breast cancers are high grade tumors with poor prognosis (Perou et al. Nature 406:747−52, 2000; Nielsen et al. Clin Cancer Res 10: 5367−74, 2004). In gene expression profiling studies, α-basic (αB)-crystallin, a small heat shock protein with anti-apoptotic and oncogenic activity, is commonly expressed in basal-like tumors. We previously reported that tumors over-expressing this protein had a poor prognosis, and that approximately half of basal-like breast cancers express αB-crystallin (Moyano et al. J Clin Invest 116:261−70, 2006). In this study, we aim to validate the prognostic value of αB-crystallin in a regional population-based series of 4000 breast cancers, powered for subset analysis.

Materials: Tissue microarrays were constructed using 4046 invasive primary breast cancers referred to the British Columbia Cancer Agency from 1986 to 1992 with clinical outcome. Breast cancer subtypes were defined using the immunopanel of ER, PR, HER2, epidermal growth factor receptor (EGFR) and cytokeratin 5/6. Immunohistohemistry of αB-crystallin was scored as diffuse positive (⩾30% of cancer cells positive), focal positive (<30% of cancer cells positive), or negative. Univariate survival probabilities were estimated using Kaplan–Meier method. Multiple Cox regression analyses and likelihood ratio tests (LRT) were used to determine the independent prognostic significance of αB-crystallin.

Results: Among breast tumors interpretable for αB-crystallin, 11% (361/3285) of cases are positive. Consistent with the previous report, 55.4% (175/316) of basal-like tumors, defined as ER/PR/HER2 negative and (EGFR or cytokeratin 5/6) positive, express αB crystallin. αB-crystallin positive tumors are associated with 11% absolute decreased breast cancer survival [10-yr BCSS (95% CI) 75% (73−77) versus 64% (58−68)]. In the Cox regression model including lymphovascular invasion, tumor size, grade, nodal involvement, age at diagnosis and breast cancer subtypes, αB-crystallin remains as an independent poor prognostic marker with a hazard ratio of 1.310 (LRT p = 0.02113). Within the subset of basal tumors, αB-crystallin positive tumors are also independently associated with poorer breast cancer survival (Hazard Ratio 1.63, LRT p = 0.02).

Conclusion: αB-crystallin independently predicts poor survival in a large population based cohort and among basal-like tumors, suggesting its role as a novel biomarker that identifies a particularly aggressive subset of basal-like tumors.

34 Poster Discussion

Monoclonal antibodies specific for Phospho-4E-BP1 (Thr 70) and phospho-AKT (Ser 473) indicate prognosis in breast cancer

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Background: The activation of cell surface growth factor receptors initiates a cascade of signalling through overlapping signalling pathways via the phosphorylation of signalling proteins. Previous studies have suggested that the phosphorylation of 4E Binding Protein 1 (4E-BP1), Mitogen Activated Protein Kinase (MAPK) and v-akt murine thymoma viral oncogene (AKT) proteins has value as a prognostic indicator in breast cancer. However these studies have been limited by small patient groups and, in some cases, complicated by the interaction of systemic treatment on outcome.

Materials and Methods: Paraffin embedded invasive tumour samples from 430 patients who had received no adjuvant chemo or hormonal therapy were used to construct a Tissue MicroArray (TMA). Median follow up was 21 years. Tissue sections from TMAs were stained using monoclonal antibodies to ER, PgR, Ki67, phospho-AKT, Phospho-4E-BP1 and polyclonal HER2 and phospho-MAPK antibodies using standard immunohistochemistry methods. Nuclear markers (ER, PgR, Ki67 and Phospho-4E-BP1 (Thr 70) were scored with validated algorithms on an Ariol imaging system (Applied Imaging). All other markers (HER2, phospho-AKT (Ser 473) and phospho MAPK (Thr202/Tyr204)) were scored manually.

Results: ER and PgR histoscores were significantly positively correlated (p < 0.001). A significant inverse correlation observed between both ER and PgR histoscores and Ki67 (both p < 0.001). Analysis indicated a significant correlation between high phospho-4EBP1 staining and reduced recurrence free survival (p < 0.05). Conversely, high phospho-AKT staining was correlated with longer overall survival (p < 0.05).

Conclusions: We have found that the phosphorylation of 4E-BP1 and AKT proteins are prognostic for disease free and overall survival respectively in breast cancer patients in the absence of systemic therapy suggesting these are true prognostic markers in breast cancer. Further analysis of their significance in the context of other known markers of breast cancer prognosis will be performed and presented.

Wednesday, 16 April 2008 12:30–14:30

POSTER SESSION

Detection, diagnosis and imaging

35 Poster

Axillary study before surgery in patients with breast cancer

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Background: The axillary study with ultrasound and cytological puncture with fine needle aspiration of suspicious nodes are new diagnostic methos.

Material and Methods: We study 159 patients with axillary ultrasound and cytological puncture with fine needle aspiration (FNA) of suspicious nodes. Suspicious nodes were those with at least one of the following signs: long to short axis ratio less than 1.5, absence of hilius and cotical disrruption. If the results were compatible with metastases (positive) then we performed axillary lymphadenectomy, if it was found to be benign (negative) then we conducted sentinel node study.

Results: In the group of ultrasound positive plus ultrasound positive FNA positive was 54 patients (33.96%) when we conducted axillary lymphadenectomy, 13 patients (24%) were found to have one positive node, 7 patients (13%) two positive nodes, 9 patients (16%) three positive nodes, 25 patients (45%) more than three positive nodes.

The other group (ultrasound negative plus ultrasound negative plus FNA negative) was 105 patients (66.03%), the sentinel node study was: in 76 patients (72.38%) pNOi−, in 9 patients (8.57%) pNOi+, in 7 patients (6.66%) pN1mic, in 12 patients (11.42%) pN1a, in 1 patient (0.95%) pN2a.

Conclusion: The axillary study with ultrasound and FNA before surgery allows excluding a group of patients to make the sentinel node study.

36 Poster

Magnetic Resonance Imaging to predict pathological response in neoadjuvant chemotherapy for breast cancer

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Background: The rationale of neoadjuvant chemotherapy in patients with locally advanced breast cancer is to achieve down-staging of the tumour to enable breast conservative surgery. The objective of this study is to