detection of the proteins at these expression levels. MRP1–3 expression was not associated with tumor response to treatment or with impaired outcome.

Conclusions: MRP1–3 are expressed in breast cancer cells, but the immunohistochemical detection failed. We have found no evidence linking these proteins to clinical drug resistance.

183 POSTER

S-HER2 by chemiluminescence versus ELISA

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The purpose was to establish corresponding discriminatory values and if possible create an algorithm for conversion of values from one to the other.

Sera from 80 cancer patients and 120 healthy controls randomly selected from the county population database were run on the Bayer Centauer HER2 chemiluminescence kit and compared to the DAKO HER2 ELISA kit.

The correlation was ELISA = 0.6508 Centauer + 1.66 ng/ml and the R2 = 0.9174.

With a discriminatory value of 15 ng/ml on the Centauer, the corresponding value was 11.8 ng/ml on Elisa.

We conclude that the results can be converted between the two, and the precision on both is sufficient for monitoring the same patient using both methods.

184 POSTER

The influence of oral contraceptives on breast cancer's mitotic activity

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Background: To correlate the administration of oral contraceptives with the mitotic activity of the breast in breast cancer patients.

Material and Methods: The correlation of previously administered oral contraceptives with the tumor's mitotic activity was investigated in 58 breast cancer patients. The PCNA (Proliferating Cell Nuclear Antigen) expression was immunohistochemically evaluated in histologic specimens of the tumor. According to the PCNA expression the tumors were divided in those of low (<20%) or high (>20%) mitotic activity.

Results: 67% of the patients were oral contraceptive users in the past and 38% of these had been using the pill for a long time (>48 months). Increased PCNA expression was ascertained in the group of patients who had been using oral contraceptives in the past ($p<0.05$). No statistically significant difference was noticed in the PCNA expression among different groups of patients according to the time period of oral contraceptive use.

Conclusions: The administration of oral contraceptives in the past might be correlated with the mitotic activity of the tumor in breast cancer patients.

Wednesday, 17 March 2004

POSTERS

Tumour cell biology

185 POSTER

Activated Akt expression in breast cancer – relationships to p53, Mdm2 and patient outcome

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Background: Activation of protein kinase-B/Akt downstream of phosphatidyl-inositol 3-kinase is mediated by oestrogen and oncogenic pathways, of which HER-2 is important. pAkt phosphorylates Mdm2 to influence its subcellular localisation and to enhance p53 cytoplasmic localisation and degradation, blocking apoptosis. This study examined expression of all activated Akt isoforms (pAkt) together with p53/Mdm2 subcellular expression in a series of invasive ductal breast cancers (IDCs), to evaluate whether *in vitro* findings were related to clinical data and the effect on outcome.

Methods: Immunohistochemical expression of pAkt, was evaluated in 103 patients with invasive ductal carcinoma and related to clinicopathology, p53 and Mdm2 subcellular expression, as well as outcome. pAkt was scored 0–3+, with 0–1+ considered negative and 2–3+ positive. A score of 3+ was considered strongly positive.

Results: pAkt was evaluable in 101 patients with a ubiquitous pattern of cytoplasmic expression in 82% of IDCs. Strong pAkt expression was evident in 24%, with 18% of breast cancers showing no activation of Akt. pAkt is more likely associated with larger tumours (P=0.02), and showed no correlation to other clinicopathologic criteria or HER-2 expression. pAkt is correlated with increasing levels of cytoplasmic p53 (P=0.01), but not nuclear p53. Activated Akt did not correlate with the subcellular localisation of Mdm2. pAkt was associated with a reduced disease-free survival (P=0.04; univariate), but was not an independent predictor in relation to the Nottingham Prognostic Index.

Conclusion: Akt has implications in breast cancer growth through mechanisms inactivating p53 that involve Mdm2. We have demonstrated that activation of Akt is associated with immunohistochemical p53 expression, which is preferentially cytoplasmic. Despite *in vitro* associations, pAkt appears to be a poor marker of HER-2 expression to suggest a greater complexity of these pathways in human cancers.

186 POSTER

Effect of zoledronate on persisting disseminated tumor cells (DTC) in the bone marrow (BM) of breast cancer patients

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Background: Adjuvant systemic therapy reduces the risk for recurrence in breast cancer by approximately 10% (Early Breast Cancer Trialists' Collaborative Group, Lancet 1998). Patients with persisting DTC in the BM after primary therapy show an increased risk for distant relapse and shortened survival (Janni et al., Cancer 2001). Adjuvant chemotherapy, however, seems to have only limited effect on DTC in dormant state (Braun et al., 2000).

Aim of this study was to investigate the therapeutic efficacy of zoledronate on the persistence of DTC in BM after completion of primary therapy.

Methods: Zoledronate was applied at 4 mg q4wx6mon (loading dose 8 mg) to 14 breast cancer patients with persisting DTC in the BM. Patients were to have completed surgery and adjuvant chemotherapy for at least 6 months and had no evidence for recurrence at this point of time. In a matched pair analysis, these patients were compared to 14 patients with DTC in the BM receiving no further therapy. The BM was re-examined after a median of 8 months (range 6.5–9.83) in the treatment group and 9 months (range 2.33–29.17) in the control group. DTC were detected by immunocytochemical staining using the pan-cytokeratin antibody A45-B/B3 and the APAAP technique.

Results: Primary tumor characteristics, i.e. tumor size (P=0.66), axillary nodal status (P=1.0) and histopathological grading (P=0.76), as well as primary surgery (P=0.23), adjuvant systemic therapy (P=0.10) and radiotherapy (P=0.36) were well balanced between both patient groups. While DTC were detected in all 28 patients at the time of first BM aspiration, no patient showed DTC in the BM after 6 months of zoledronate therapy. In contrast, persisting DTC were detected in 4 patients (29%) without treatment (P=0.03).

Conclusion: These preliminary results indicate potential antineoplastic effect of the cell-cycle independent agent zoledronate on persisting DTC in dormant state. In our view, these data provide a hypothesis generating basis to investigate the therapeutic efficacy of zoledronate on DTC in a secondary adjuvant setting by prospectively randomised trials.

187 POSTER

The enhanced expressions of CxCR4 and CCR7 mRNA in breast cancer tissue do not always correlate with cancer metastasis

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Backgrounds: Cancer metastasis is a major prognostic factor for breast cancer patients. The recent findings indicated that the chemokine receptors CxCR4 and CCR7 which found on breast cancer cells, and their ligands that highly expressed at sites have an association with breast cancer metastases.

The aim of the present study was to measure CxCR4 and/or CCR7 mRNA expression in the clinical specimens of primary breast cancer, and to explore whether CxCR4 and/or CCR7 mRNA expression in breast cancer correlate with cancer metastasis and other conventional clinicopathological parameters.