Vol 23, No 16S, Part I of II June 1, 2005

— SUPPLEMENT TO —

# JOURNAL OF CLINICAL ONCOLOGY

## 2005 ASCO Annual Meeting Proceedings



41st Annual Meeting

630 General Poster Session, Mon, 2:00 PM - 6:00 PM

**Serum 25 hydroxyvitamin D levels in early and advanced breast cancer.** *C. Palmieri, T. Macgregor, S. Girgis, D. M. Vigushin; Charing Cross Hosp, London, United Kingdom; Imperial Coll London, London, United Kingdom*

**Background:** Laboratory and epidemiological studies have implicated vitamin D deficiency in the pathogenesis of breast cancer. 1,25-dihydroxyvitamin D ($1,25(OH)_2D$) promotes differentiation and apoptosis, and potently inhibits proliferation of malignant breast epithelial cells in culture. Breast cancer incidence and mortality are both increased in countries at high latitudes and increased skin pigmentation is associated with more aggressive breast cancers Decreased exposure to effective solar radiation resulting in reduced cutaneous synthesis of vitamin $D_3$ is the likely mechanism. Conversely, vitamin D sufficiency and exposure to sunlight reduce the risk of developing breast cancer and serum levels of $1,25(OH)_2D$ are higher in normal women compared to patients with primary breast cancer. This study aims to clarify the role of vitamin D in breast cancer progression by comparing the levels of serum vitamin D in patients with early and advanced breast cancer. **Methods:** Circulating levels of 25 hydroxyvitamin D 25(OH)D, parathyroid hormone (PTH), and calcium were measured in 279 caucasian women with invasive breast cancer, 204 with early stage malignancy and 75 with locally advanced or metastatic disease. Patients with renal impairment or receiving bisphosphonate therapy were excluded. **Results:** Patients with early stage breast cancer had significantly higher circulating levels of 25(OH)D ($P=0.0049$) and significantly lower PTH ($P=0.0001$) levels compared to those with advanced disease. Calcium levels did not differ significantly between the two groups ($p=0.74$). **Conclusion:** Serum levels of 25(OH)D are significantly higher in patients with early stage breast cancer compared to those with locally advanced and/or metastatic disease. The potential clinical implications of monitoring and/or maintaining high circulating vitamin D levels in breast cancer patients remain to be elucidated.

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**Quantitative monitoring of circulating epithelial cells for individual therapy control in lung and breast cancer during neoadjuvant treatment, surgery and adjuvant chemotherapy.** *K. Pachmann, J. H. Clement, K. Hoeffken, C.-P. Schneider, K. Lobodasch, O. Camara, U. Pachmann; Clinic for Internal Medicine II, Jena, Germany; Zentralklinikum Bad Berka, Bad Berka, Germany; DRK Krankenhaus Chemnitz Rabenstein, Chemnitz, Germany; Friedrich Schiller Univ Jena, Jena, Germany; Transfusionsmedizinisches Zentrum Bayreuth, Bayreuth, Germany*

**Background:** A universal characteristic of solid tumors is poor penetration into and distribution of chemotherapeutic agents in the tumor tissue due to interstitial hypertension. Individualized tumor cells shed from the tumors or seeded into the circulation before and at different times of manipulation and therapy may be better accessible and their reduction, therefore, better represent the sensitivity of the tumor. The number of circulating tumor cells can be monitored real-time using the MAINTRAC method and correlated to the extent of manipulation, tumor size reduction in the neoadjuvant and relapse in the adjuvant setting. **Methods:** Whole blood samples from patients were stained for epithelial cells using fluorochrome-labeled anti human epithelial antibody and positive events quantified using combined laser scanning cytometry and visual verification before each therapy cycle, before and 3, 7 and 14 days after surgery and at different times after completion of therapy. **Results:** The reduction in number of circulating epithelial antigen positive tumor cells during the first three to four cycles very closely reflected the response of the whole tumor to neoadjuvant therapy ($R^2= 0.6–0.9$). Later massive release of tumor cells from disintegrating tumor tissue occurred into circulation remaining even after surgery which frequently lead to an additional spike of circulating epithelial cells, possibly a mixture of normal and live and dying tumor cells. They were only partly removed during further therapy and cells could be detected in the circulation even after months to years presumably the live tumor cells. Adjuvant therapy reduced the number of circulating epithelial cells. An increase in such cells during or subsequent to therapy was a statistically significant predictor of relapse. **Conclusions:** Tight monitoring of circulating epithelial/tumor cells from peripheral blood provides so far unexpected insights into the interrelationship between circulation and tumor and may become an important tool for monitoring therapeutic interventions in solid tumors.

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**The clinical impact of proliferative high-risk lesions presenting concurrently with ductal carcinoma in situ (DCIS) in patients (pts) treated with breast conserving therapy (BCT).** *L. J. Adepoju, W. F. Symmans, G. V. Babiera, S. E. Singletary, N. Sneige, T. A. Buchholz, K. K. Hunt, F. Meric-Bernstam, B. Arun, H. M. Kuerer; MD Anderson Cancer Ctr, Houston, TX*

**Background:** Atypical ductal hyperplasia (ADH), atypical lobular hyperplasia, and lobular carcinoma in situ (ALH/LCIS) are associated with an increased risk of development of breast cancer. The clinical significance of a concurrent diagnosis of ADH and or ALH/LCIS with DCIS in pts treated with BCT is unknown with respect to risk of local recurrence and subsequent risk of contralateral breast cancer (CBC). **Methods:** Following IRB approval, 313 pts were identified from our prospective institutional database. Pts were treated with BCT from 1968 to 1999 for a diagnosis of DCIS and their complete medical records were analyzed with particular attention to pathology reports noting the presence of ADH or ALH/LCIS within the tumor or within normal adjacent tissue. Actuarial local recurrence rates were calculated by the Kaplan-Meier method and differences between groups were tested using the log-rank test. **Results:** Median follow-up time was 94 months. Of the 313 pts with DCIS, 73 also had ADH, 27 also had ALH/LCIS and 12 also had both ADH and ALH/LCIS. Ten-year ipsilateral local recurrence was 7.93% for pts with ADH, ALH/LCIS, or both compared with 13.8% for pts without these lesions ($P=0.39$). The rate of CBC development in pts with a diagnosis of DCIS with concurrent ADH was 3 times greater than pts with a current diagnosis of DCIS alone ($P<0.01$). The cumulative risk of CBC development was 10.7% in pts with a diagnosis of DCIS and ADH compared with 3.52% in pts with DCIS alone ($P<0.01$). Pts with a diagnosis of DCIS and ADH or ALH/LCIS also had a statistically higher rate of contralateral breast cancer prior to their diagnosis of DCIS compared to pts without these proliferative lesions (11.76% vs. 5.26%, $P=0.04$). **Conclusions:** The additional risk of development of CBC associated with a diagnosis of DCIS alone compared with a concurrent diagnosis of DCIS and proliferative breast lesions has not been previously reported. Pts with this clinical entity may be appropriate candidates for additional chemoprevention strategies. The presence of ADH and ALH/LCIS in pts with DCIS does not preclude BCT.

633 General Poster Session, Mon, 2:00 PM - 6:00 PM

**Serial FDG-PET to monitor treatment of bone-dominant metastatic breast cancer predicts time to progression (TTP).** *S. L. Tam, J. R. Gralow, R. B. Livingston, H. M. Linden, G. K. Ellis, E. K. Schubert, L. K. Dunnwald, D. A. Mankoff; Seattle Cancer Care Alliance, Seattle, WA; Univ of Washington, Seattle, WA*

**Background:** The response of bone-dominant breast cancer to therapy is difficult to assess by conventional imaging approaches such as bone scan and MRI. Our preliminary studies have previously shown that quantitative serial [F-18]-2-fluoro-D-glucose positron emission tomography (FDG PET) correlates with therapeutic response of bone-dominant breast cancer, but the relationship to long-term outcome measures is unknown. The aim of this study is to evaluate the prognostic power of FDG PET imaging in bone-dominant breast cancer undergoing treatment. **Methods:** A retrospective analysis was performed on the medical records of 405 breast cancer patients who were previously referred for FDG PET between January 1999 and December 2003. From this population of patients, 29 patients were selected who demonstrated metastatic bone only +/- nodal breast cancer and were undergoing treatment with at least 2 serial PET scans which had clear uptake. The standard uptake value (SUV) changes for the most conspicuous bone lesion were compared to long-term prognostic outcomes (TTP, time to skeletal-related event(t-SRE), and time to death(TTD)). Time-to-progression was defined as the time from the initial index FDG PET to disease progression (>25% increase in tumor markers, clear symptomatic progression, progression on some other imaging modality, skeletal-related events, or a new lesion). A skeletal-related event was defined by hypercalcemia, radiation therapy to stabilize disease, pathologic fracture, cord compression, or surgery to stabilize spine. **Results:** Using hazard analysis, longer TTP correlated with greater decreases in SUV either by absolute or percentage changes. T-SRE was found to significantly correlate with higher initial SUV readings. In addition, when grouped by tertiles for absolute SUV changes, the smallest and largest tertile groups correlated with t-SRE. No correlation was demonstrated for TTD and SUV changes, however only one death occurred during this study analysis. **Conclusions:** Preliminary results indicate that serial FDG PET predicts TTP and t-SRE in bone-dominant breast cancer; however, larger prospective trials are needed. Supported by CA72064, CA42045, and BCRF