improvement and strategies are being implemented to change this picture. A large national breast cancer project is being planned and soon will incorporate screening mammography after the age of 50.

The increasing costs associated with treatment add to the burden of dealing with breast cancer in Brazil. Currently, breast cancer represents approximately 1/4 of the Government costs with systemic treatment (chemotherapy and hormonal therapy) in cancer.

In summary, breast cancer incidence and mortality are increasing in Brazil. During the next decade, the main challenge will be the development of a coherent strategy for its management based on detection at an earlier stage.

Thursday, 18 March 2004 16:00–17:15

PROFFERED PAPERS

Advanced disease

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Gene expression profiles of primary breast tumors maintained in lymph node- and distant metastases

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Background: Metastases at distant sites are the main cause of death in breast cancer. It is largely unknown whether the characteristics of breast cancer that define the growth rate and therapy response of the primary tumor are alike in the metastases. Furthermore, it is still unclear whether metastases derive from highly metastatic subpopulations of tumor cells within the primary site, or whether they originate from a random fraction of tumor cells. To test this, we compared pairs of human primary breast carcinomas and their lymph node metastases as well as primary breast tumors and their metastases developed years later at distant sites, both by gene-expression profiling.

Patients and methods: Surgical specimens of primary breast tumors and their matching lymph node metastasis of 15 patients, and specimens of primary breast carcinomas and their matching distant metastasis from different localizations of eight patients were collected from the frozen tissue bank of our hospital. RNA from these tissues was isolated, DNase treated and cRNA was generated using T7 RNA polymerase. Fluorescently labeled cDNAs were hybridized to an 18k human microarray (Central Microarray Facility, Netherlands Cancer Institute). Intensities of scanned images were quantified, normalized and ratios were calculated and compared to the intensities of a reference pool. Gene clustering and tumor clustering were performed using an unsupervised hierarchical clustering algorithm (Pearson correlation coefficient).

Results: We show, by gene-expression profiling, that human primary breast tumors are strikingly similar to their regional lymph node metastases as well as to their distant metastases of the same patient. Unsupervised hierarchical clustering, multidimensional scaling, permutation testing, as well as the comparison of significantly expressed genes within a pair, reveals their genetic similarity.

Conclusions: Our results show that the molecular program established in a primary breast carcinoma is not only highly preserved in its regional lymph node metastasis but also in its distant metastasis. These findings suggest that metastatic capability in breast cancer is an inherent feature, and is not based on clonal selections. The results further imply that neo-adjuvant treatment given to patients based on the response expression profiles of their primary breast tumor might also prevent the outgrowth of micrometastases.

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The clinical and prognostic implications of isolated supraclavicular fossa recurrence

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Introduction: In 2003, AJCC changed the classification of breast supraclavicular fossa (SCF) node metastasis. This is now classified as stage 3C. We have reviewed our experience in the light of these changes.

Methods: Review of case notes and database of 8691 patients with a diagnosis of breast cancer and either isolated ipsilateral or contralateral SCF metastasis. All patients had completed treatment for primary breast cancer and had no previous evidence of metastatic disease. Patients diagnosed with metastatic disease at other sites either at the time of SCF recurrence or within the next three months were excluded.

Results: There were 125 cases of ipsilateral (I-L) SCF recurrence (SCFR) and 22 separate cases of contra-lateral (C-L) disease. The median time from primary diagnosis to SCFR was 1.92 yrs for I-L disease and 3.32 years for C-L (p=0.0229). Patients had originally presented with node positive cancer in 79% of cases (I-L 80%, C-L 73%, p=0.58) and locally advanced disease in 9.5% (I-L 8.8%, C-L 13.6%, p=0.75). 57% were primary invasive ductal carcinomas, 3% infiltrating lobular carcinomas and 40% other types. At diagnosis 2.5% were grade 1, 46% grade II and 52% grade III. There was no significant difference in tumour type or grade between I-L and C-L. Treatment for SCF recurrence comprised combinations of chemo and hormonal and radiotherapy. Median time to first relapse after SCF recurrence was 11 months. Sites of first relapse were lung in 16%, pleura 9%, bone 8%, liver 10%, skin 7%, brain 3%, mediastinum in 3%, ascites in 2%, local breast recurrence in 31%, and other mets in 18%. The median time from SCF recurrence to death not significantly different between C-L (1.89 yrs) and I-L (2.63 yrs, p=0.184) recurrence. There were no patients who did not eventually die from their disease (survival = 0%), but 15% were still alive at 5 yrs (3/22 C-L and 19/125 I-L), and 3.4% at 10 years (0/22 C-L and 5/125 I-L). Median survival was 25 months for chemotherapy alone (12.2%), 28.3 months for those treated with combined RT and systemic (hormonal and/or chemotherapy) and 40.6 months for hormonal therapy (21.1%).

Conclusion: This is the largest published series of SCF recurrence. It demonstrates that SCF recurrence is associated with subsequent systemic metastases and eventual death in 100% of cases. I-L disease is diagnosed at an earlier stage than C-L, but both have a similarly poor prognosis. SCF recurrence might be better regarded as stage IV disease.

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Trastuzumab (Herceptin®) plus docetaxel versus docetaxel alone as first-line treatment of HER2-positive metastatic breast cancer (MBC): results of a randomised multicentre trial

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Background: The H0648g trial showed a significant survival benefit for Herceptin (H) plus paclitaxel compared with paclitaxel alone, and as a result the combination is licensed for the treatment of HER2-positive MBC as first-line therapy. Phase II studies have shown that the combination of Herceptin plus docetaxel (HD) is also active in patients with HER2-positive MBC. A large, multicentre randomised trial (M77001) was conducted to compare HD versus docetaxel alone (D) as first-line therapy in HER2-positive MBC.

Patients and methods: 188 patients (pts) with HER2-positive MBC and at least one measurable lesion were randomised to either HD or D given as first-line treatment. Two pts in the HD arm received no study treatment and were excluded from analysis. Ninety-five percent of pts had IHC 3+ and/or FISH-positive disease. Herceptin dosing was 4 mg/kg iv (loading) followed by 2 mg/kg weekly until disease progression, and docetaxel 100 mg/m^2 iv q3w $\times$ 6 cycles. Patients progressing on D alone were allowed to cross over to receive H. Response was assessed according to WHO criteria and radiologically confirmed by an independent review board. Patient demographics were generally balanced between the arms, although more D than HD pts were hormone-receptor positive (56% v 41%), and more HD than D patients had received adjuvant anthracyclines (64% v 55%).

Results: At 12 months after last pt enrolment, efficacy in the HD arm was significantly better than in the D arm: overall response rate 61% v 34% (p=0.0002); median time to progression 10.6 v 5.7 months (mo) (p=0.0001); median duration of response 11.4 v 5.1 mo (p=0.0011). Survival was significantly superior for HD (p=0.0062) (median overall survival 30.5 mo in the HD arm v 22.1 mo in the D arm), despite at least 48% of pts in the D arm crossing over to receive H. Pts who crossed over from D to receive H had a longer estimated median survival (24.5 mo) than those who did not cross over (19.1 mo). Grade 3/4 non-haematological toxicity was similar in the two arms. The incidence of febrile neutropenia was slightly higher in the HD arm (23%) than the D arm (17%) but was generally manageable; two septic deaths occurred in the D arm. Symptomatic heart failure occurred in 2 pts in the HD arm (2%), but both cases were in the