q 3 wks (FLN regimen). Seventy-six patients received 5-fluorouracil 200 mg/m2/die as intravenous continuous infusion, vinorelbine 20 mg i.v. as total dose on days1 and 3, plus cisplatin 60mg/m2 i.v. on day 1 q 3 wks (ViFuP regimen).

Results: The overall response rate (partial and complete remissions) according to radiological and clinical evaluation was 65% (95% C.I: 57%-72%.) In both the univariate and multivariate analyses the most important predictive factor was the baseline absence of expression of PgR ($p<0.01$), high baseline Ki-67 ($p<0.01$) and decrease of p53 positive cells ($p<0.01$). Conversely no significant effect according to other histological features was observed.

Conclusion: Our results indicated that baseline PgR and Ki-67 expression as well as changes during therapy of p53, should be considered in further studies on preoperative chemotherapy.

656 POSTER

Effect of elevated serum carboxyterminal telopeptide (ICTP) on survival in breast cancer patients with and without bone metastases

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Purpose: Bone is made of Type I collagen fibrils that are crosslinked e.g. by pyridinium cross-links. Bone resorption releases the cross-links as free and peptide bound (telopeptide) fragments. There are 2 assays available for the carboxy-terminal telopeptide fragments, ICTP and Crosslaps. ICTP elevations have also been seen in non-bony disease and found to be prognostic in ovarian cancer patients. We evaluated the prognostic value of serum ICTP levels in patients without bone metastasis (BM-) and with bone metastasis (BM+).

Methods: ICTP levels were quantified in serum using an ICTP RIA produced by Orion Diagnostica (Espoo, Finland) and distributed in USA by Diasorin, Inc. (Stillwater, Minn). This was a retrospective study and used baseline serum that was obtained from 253 patients with metastatic breast cancer. These patients had participated in a double-blind randomized study of second-line hormonal therapy with a second-generation aromatase inhibitor (Fadrozole) vs. Megace.

Results: The mean followup for survivors was 868 days (range 264 - 1466). Normal serum ICTP level from a published report of 202 healthy postmenopausal women was 3.0 + 1.6 ug/L (mean + SD). The serum ICTP cutoff of 6.2 ug/L was established using the mean + 2 SD. Using this cutoff, 62/181 patients (34%) in the BM+ group had elevated serum ICTP levels as compared to 6/72 (8%) in the BM- group. Mean serum ICTP for the BM+ group [6 ug/L (1.7 - 24.6)] was significantly higher compared to the BM- group [4.2 ug/L (1.6 - 16.1)]($p= 0.0002$). Overall survival was significantly worse in patients who had elevated baseline serum ICTP levels in both the BM- ($p=0.02$) and BM+ groups ($p<0.0001$).

Conclusion: In summary, an elevated serum ICTP level predicts for decreased survival in breast cancer patients with and without clinically-detectable bone metastasis.

657 POSTER

KI67 and p53 are not predictive of tumor response or survival with trastuzumab-based therapy in metastatic breast cancer patients (pts) with her2/neu-overexpression

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From 2/99 to 3/01, 53 pts with metastatic breast cancer overexpressing HER2/neu were treated with trastuzumab alone (25 pts, group A) or in combination with chemotherapy (28 pts, group B). 3+ -positive HER2/neu overexpression was determined with immunohistochemical staining using antibodies (Ab) 3b5 or A0485. In group B, 19 pts received docetaxel, 5 pts paclitaxel, 2 pts vinorelbine, and 2 pts mitomycin/5-fluorouracil. Pts have been treated either as first-line therapy (17 pts), or as second-line (26 pts) or as third line (10 pts). Using immunohistochemistry staining on primary tumor sections, 23 of 40 pts (58%) showed equal or more than 35% KI67 positive cells (Ab MIB-1) and 17 pts showed equal or more than 50% p53 positive cells (43%, Ab DO7). KI67 and p53 expression in tumor cells were well balanced between groups A and B. To evaluate the predictive value of KI67 and p53 for response, chi-square tests were performed. The predictive value for survival was determined by univariate analysis (log-rank test). The overall response rate (ORR = CR + PR) and the clinical benefit rate (CBR = CR + PR + SD > 24 weeks) were 36% and 60% (group A: 48% and 76%; group B: 25% and 46%), respectively. After a median follow-up of 35 weeks (w) (range, 3 -93 w) the median progression-free survival (PFS) and overall survival (OS) were 25+ w (range, 2-93 w) and 35+ w (range, 3 -93 w) so far. Pts with high or low levels of KI67 or p53 positive tumor cells showed no difference in response rates (ORR: pKI67=0.84, pp53=0.21; CBR: pKI67=0.69, pp53=0.55) and survival rates (PFS: pKI67=0.72, pp53=0.79; OS: pKI67=0.58, pp53=0.56).

In conclusion the proportion of KI67 and p53 positive tumor cells on primary tumor sections might not predict response or survival for a trastuzumab-containing therapy in pts with HER2/neu overexpressing metastatic breast cancer.

658 POSTER

Upstaging of breast cancer patients with PT1 tumours by detection of micrometastasis in sentinel lymph node biopsy (SLND)

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Purpose: Determination of axillary lymph node status is an integral part for patients with early breast cancer and the most important prognostic factor. 15-20% of patients with tumour-free axillary lymph nodes in conventionel H&E staining show recurrences and distant metastasis within 10 years. Serial sectioning and immunohistochemistry (IHC) of the sentinel lymph nodes (SLN) allow more accurate information about micrometastasis (≤2 mm)

Methods: Between September 1997 and April 2001 114 patients with pT1 breast carcinoma were prospectively enrolled and underwent SLND with tumour resection. SLN were detected using blue dye and/or 99mTc labeled colloidal tracer. Completion axillary lymphadenectomy of level I and II was performed in case of macrometastasis in the SLN. Sentinel nodes were examined by serial sectioning and IHC (Lu-5/CK22).

Results: SLN were identified in 108 (95%) of 114 patients. 37 (34%) patients with a pT1 tumour had a SLN metastasis, 71 (66%) being tumour-free. In 14 (38%) cases SLN contained micrometastasis, diagnosed by serial sectioning with H&E staining and by IHC in 7 patients each. 23 (62%) patients had macrometastasis. 12 of 14 micrometastasis and 22 of 23 macrometastasis in SLN were found in patients with pT1c tumours.

Conclusion: In our previous study we reported an incidence of axillary lymph node metastasis in pT1 tumours of 25% without SLN (n=185). Serial sectioning and IHC of SLN lead to an upstaging of one third in this group. Further studies are necessary to assess a potential benefit of ALND in this subgroup of breast cancer patients.

659 POSTER

Sentinel lymph node biopsy and axillary dissection in breast cancer: results and initial experience of a changed technique with subareolar intradermal blue dye injection only

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Introduction: Our study tries to assess the value of intraoperative efficacy to identify the sentinel lymph node in clinical management of breast cancer. We hypothesized that the axillary lymphatic drainage pattern in predicting the pattern of metastatic spread from primary breast carcinoma is independent from a particular breast quadrant and it might be useful to examine our hypothesis in using subareolar intradermal blue dye injection only.

Methods: Between 5/99 and 12/2000 we investigated 86 consecutive patients (85 women, 1 men) using 2 ml of Lymphazurin 1%, which was injected intra- and subdermal into the subareolar area, immediately before definitive surgical treatment of primary breast carcinoma without massage of the breast. The average age of the patients was 59 years (range37-83).In these 86 patients we performed peritumoral blue dye injection in 13 cases, intradermal subareolar injection in the remaining 73 cases. Out of these we found verification of breast cancer in 60 cases, in which complete axillary lymphadenectomy was done and 13 cases with DCIS and/or no completed axillary dissection.